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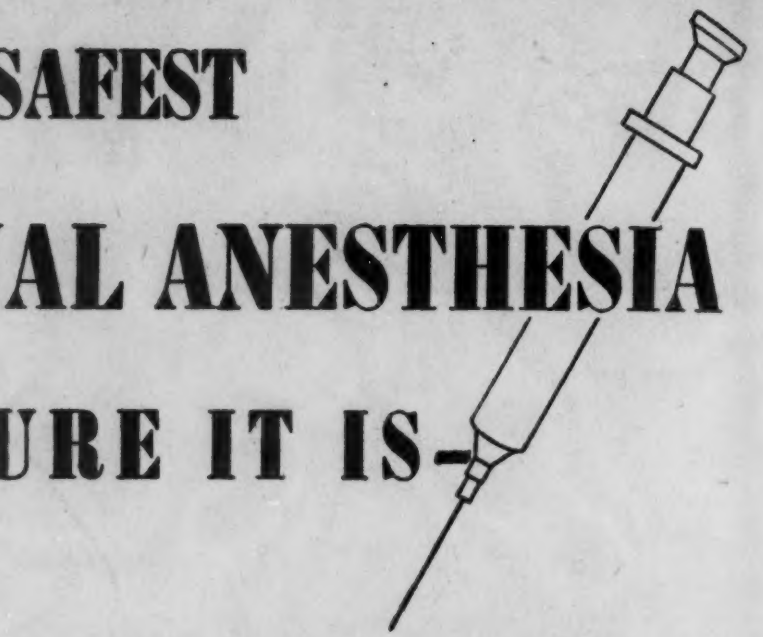

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ANNALS OF SURGERY

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EARLY SKIN GRAFTING IN WAR WOUNDS OF THE EXTREMITIES *

JOHN MARQUIS CONVERSE, M.D.

NEW YORK, N. Y.

FROM THE DEPARTMENT OF PLASTIC SURGERY, AMERICAN HOSPITAL IN BRITAIN, OXFORD, ENGLAND

INJURIES OF THE EXTREMITIES occurring in modern warfare often produce wounds with extensive skin losses creating special problems. These skin losses may be due to extensive lacerations by glass or other flying materials due to bomb explosion. Large flaps of skin may be avulsed by bomb blast. Bomb fragments hitting bone create an explosive effect with marked tissue destruction. Deep burns destroying skin have been frequent, due to the great development of mechanized warfare, and the ever increasing use of incendiary bombs.

The characteristic wound seen in air raid casualties is produced by crushing. The patient is crushed by falling building materials causing multiple injuries and compound fractures. Localized thrombosis and gangrene of whole areas of tissue occur—these areas later separate as sloughs.

These wounds may show skin destruction tending to encircle the limb. Following the spontaneous healing of such a wound constriction may result causing circulatory disturbances in the extremity.

The skin destruction may be situated near a joint. Contractures limiting the function of the articulation may be the sequela of such a wound.

In compound fractures, one or many wounds may be found either in direct relation to the fracture site or in the proximity of the fracture. When the wound presents considerable loss of superficial tissue, healing may be incomplete and of poor quality; thus giving an inadequate covering to the fractured bone. Infection may delay healing and consolidation of the fracture. Under plaster such a wound is a natural culture medium, and may discharge an abundant and fetid, purulent exudate of rich and varied bacterial flora. Great delay in the performance of important secondary bone, nerve or tendon surgery may be due to the presence of an unhealed wound under plaster.

When bone is exposed through the loss of superficial covering and perios-

* Read before the Royal Society of Medicine (Section on Orthopedics).

teum, it becomes devitalized, sequestrated, and is open to infection and osteomyelitis. Tendon left uncovered is destined to slough.

To restore normal function to the extremity, in many of these cases, extensive secondary plastic reconstructive operations are often necessary, further delaying the patient's return to active work. It is felt that many of these late complications could be avoided by the early replacement of the skin loss.

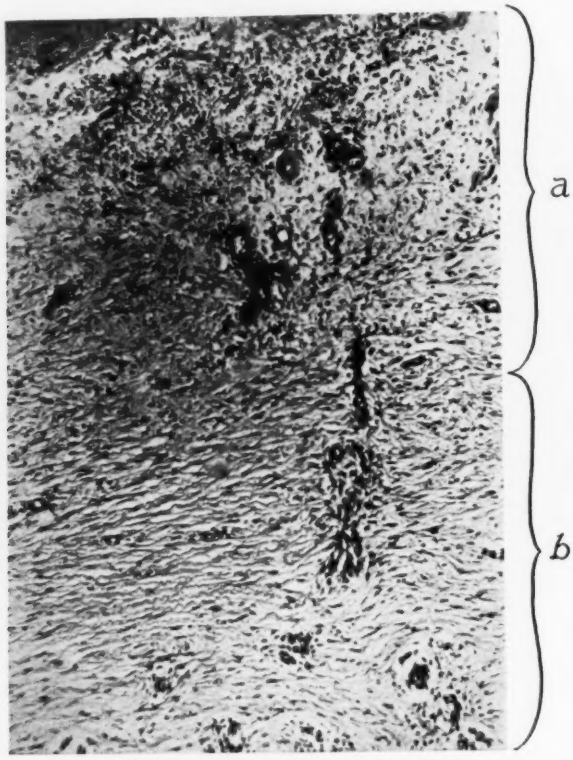


FIG. 1.—Section of three-month-old granulation tissue showing development of deep fibrous tissue. (a) Chronic inflammatory granulation tissue. (b) Deep fibrous tissue layer.

Pathology of the Unhealed Wound.—The importance of early wound epithelization is brought out by the study of the changes that occur in a wound failing to present rapid spontaneous healing.

In normal wound healing a double regenerative process occurs—that of connective tissue and that of epithelial tissue. Healing is not achieved until the new connective tissue, known clinically as granulation tissue, is covered by a continuous layer of new epithelium. Sections made of young granulation tissue show numerous newly-formed blood vessels and fibroblasts. The latter are situated in a parallel fashion to the blood vessels.

In older granulation tissue, often in wounds, even as early as three to four weeks old, towards the base of the layer of granulation tissue the fibro-

blasts assume a more horizontal direction, thus tending to be perpendicular to the blood vessels. At the same time between the fibroblasts appear connective tissue fibers and collagen (Fig. 1).

As the unhealed wound grows older, this deep layer of fibrous tissue tends to increase at the expense of the superficial layer of granulations. Large numbers of capillaries are obliterated, thus depriving the superficial layer of granulation tissue of some of its blood supply. The granulations tend, clinically, to appear cyanotic and edematous due to venous congestion. This first evidence of impaired circulation is improved by pressure over the wound.

The deep fibrous layer slowly invades the superficial granulation tissue, the surface of which tends to become necrotic through defective circulation and secondary infection. Finally, the whole wound tends to become a mass of fibrous tissue.

It can thus be seen that the pathologic picture of an unhealed wound is one of gradually diminishing blood supply, and of progressive increase of fibrous tissue. This produces an increasingly unfavorable base for the spread of epithelium and predisposes the wound to secondary infection.

Rôle of Infection.—Infection by pathogenic organisms lead to wound suppuration. The presence of pus appears to be detrimental to epithelial growth, in general. Furthermore, certain organisms seem to have a specific inhibiting action on new epithelium. This is particularly true of various types of streptococci. Colebrook and Francis[1] have reported the remarkable growth of epithelium following the disappearance of the streptococcus from superficial wounds after local applications of sulfanilamide powder.

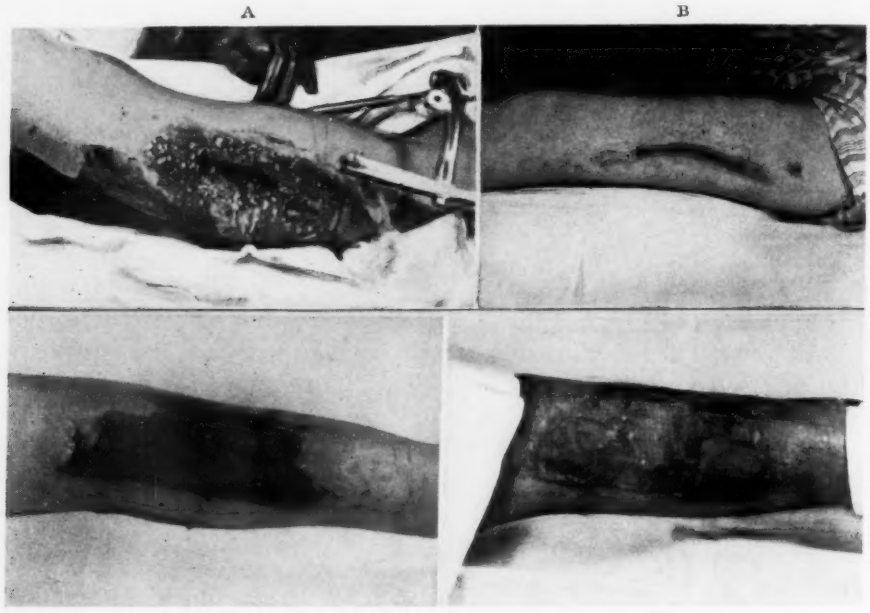
In the stage of acute inflammation, the accompanying edema may prevent the occurrence of contraction, which is a very important phenomenon in wound healing.

Importance of Wound Contraction.—Contraction of the wound takes place early in the process of healing, and continues during and after epithelization. Primary contraction occurs following a "silent" or "lag-period" during which, through phagocytosis, the elaboration of enzyme, and exudation of lymph, the wound rids itself of devitalized tissues and foreign bodies. Its occurrence is greatly hastened by the surgical removal of the destroyed tissues by débridement. This contracture is probably due to pull of the elastic fibers within the connective tissue in and around the wound. It is an effort to make the wound smaller, and close it off from the surrounding tissue.

Secondary contraction takes place later in the process of wound healing. When the unhealed wound is invaded by fibrous tissue, connective tissue cells and collagen appear. Contraction proceeds slowly and may continue even after epithelization. The progressive contraction along a scar-line is well known. This late contraction tends to bring the epithelial edges of the wound closer together and is the cause of constrictions, contractures, and deformities of the extremities. The longer the wound remains unepithelized the more marked these deformities will become.

Primary contraction constitutes one of the most important elements of wound healing. It greatly diminishes the size of the wound that is to heal. The defect in deep wounds is filled by surrounding tissue and muscles being "pulled in" as a result of tissue contraction.

Primary wound contraction is such an important element of wound healing that it is possible, to a certain extent, to predict the rapidity and the quality of the wound repair according to whether the wound is situated in a position favorable or unfavorable for wound contraction. Contraction occurs best



Top.—FIG. 2.—(A) Extensive wound of thigh in compound comminuted fracture of femur due to bomb fragment. (B) Example of healing by contraction of wound shown in (A), eight months after injury.

Bottom.—FIG. 3.—(A) Wound of compound fracture of tibia after four months' treatment in closed plaster. Note absence of epithelization. (B) Healing obtained by secondary débridement and skin grafting at time of change of plaster.

when muscle tissue is abundant. Thus, it can be stated that, in a general way, contraction and consequently wound healing are directly proportional to the amount of muscular tissue around the wound. To cite the lower extremity as an example, wounds of the thigh generally heal well, while wounds of the anterior tibial region heal poorly (Figs. 2A, 2B, 3A and 3B).

The size of the wound has a bearing on the evolution of healing. Epithelial regeneration through a process of cellular enlargement, multiplication and migration, proceeds at a certain rate. If the loss of tissue is large and if it is in an unfavorable situation for contraction, epithelization of the wound will take a certain length of time during which the fibrous changes, previously described, may occur. It is frequent to see large wounds over the tibia healed but covered by epithelium resting on poorly vascularized fibrous tissue. This poor covering for the bone, which is destined to break down,

appears to bear some of the responsibility for the chronicity of osteomyelitis of the tibia.

The "Vicious Circle" of the Unhealed Wound.—Where the skin loss is extensive, and when wound contraction is poor, fibrous tissue develops. The circulation of the wound is impaired and infection occurs. Epithelial growth is retarded and more fibrous tissue is deposited. This cycle can repeat itself indefinitely. The result is an unhealed wound.

From these considerations, one is led to conclude that the rapid covering of the wound by epithelium is desirable. If spontaneous epithelial regeneration appears difficult, it is preferable to resort to the artificial provision of epithelium through skin grafting.

INDICATIONS FOR SKIN GRAFTING

A skin grafting opreation should be considered:

(1) *When the skin loss is such that it appears probable that impairment of function of the extremity will result.*

This applies particularly to wounds about the joint surfaces and to wounds which tend to be circular and are liable to cause contractures and circulatory difficulties.

(2) *When spontaneous healing of the wound appears improbable.*

In the aged and debilitated when the wound is in an unfavorable anatomic situation for healing.

(3) *When rapid healing is desirable.*

Skin grafting makes possible at an earlier date secondary operations such as nerve suture or grafting, secondary tendon suture, or secondary bone surgery. In such cases epithelial healing may be achieved in 10 days, when spontaneous epithelization may be prolonged for months. Thus, one is led to feel that skin grafting is justified whenever there is an appreciable skin loss.

SKIN GRAFTING OF OPEN GRANULATING WOUNDS

A study was made of 110 skin grafting operations performed between October, 1940 and June, 1941, at Rooksdown House, and the American Hospital in Britain, Park Prewett Hospital, upon infected granulating wounds. Records were kept of the date and cause of the injury, the date of the skin grafting operation, the bacteriology of the wound before and after operation, and the percentage of success of the skin graft. One hundred per cent represented a complete "take." The operative procedure and postoperative follow-up were noted. Skin grafting was undertaken from two weeks to nine months after injury.

Aside from technical details of fixation of the graft, adequate pressure, etc., two main factors were found to influence the success of the skin grafting: (1) Wound infection; and (2) wound fibrosis.

(1) *Wound Infection.*—Infection creates suppuration. Purulent exu-

date will lift the graft away from the wound, thus preventing its adherence and "take." Failure, due to suppuration, may be due to the presence of any of the pathogenic organisms. Certain organisms appear to have a specific action upon the "take" of the graft. In the presence of an acute hemolytic streptococcic infection (untreated by specific chemotherapy) skin grafting is generally unsuccessful. Coincident with signs of acute inflammation the wound is filled with serosanguineous pus which displaces the graft from its bed. A dissolution of the layer of fibrin which causes the adherence of the graft appears to take place. This is probably due, as suggested by Colebrook, to a fibrolysin of the streptococcus. A late ulcerative action is observed frequently in grafts that have appeared successful. This is usually found to be due to the hemoyltic streptococcus. If uncontrolled it may destroy the whole graft.

The advent of chemotherapy has allowed great control over the hemolytic streptococcus. By the use of local chemotherapy it has become possible to obtain streptococci-free wounds, usually within a few days after initiation of

TABLE I

LOCAL CHEMOTHERAPY AND SKIN GRAFTING OF HEMOLYTIC STREPTOCOCCUS (TYPE-A) INFECTED WOUNDS

Total Number of Cases—81

	No. of Cases	Per Cent Skin Graft "Take"
(1) Failures due to absence of use of local chemotherapy during skin grafting	12	0–25
(2) Failures due to sulfonamides—resistant strain of hemolytic streptococcus	9	0–25
(3) Successful skin grafts in hemolytic streptococcus infected wounds, following secondary débridement and local chemotherapy	5	0–70
(4) Successful grafts in wounds previously freed of hemolytic streptococcus by local chemotherapy, grafted following secondary débridement and local chemotherapy	55	93
Total	81	

treatment. The wound is freed of purulent exudate by means of dressings, baths, and mechanical irrigation. The bacteriostatic action of sulfanilamide powder applied locally can then take place.[1] After this treatment, it has been possible to perform skin grafting upon wounds presenting cultures free of hemolytic streptococci.

A sulfanilamide-resistant streptococcus persisted in nine patients. Skin grafting performed in the presence of this organism was generally unsuccessful.[2]

At the time of the skin grafting, sulfanilamide powder was blown over the wound before application of the graft in most cases. The drug was insufflated as a thin layer of powder with Pearce's insufflator. No evidence could be found that the presence of sulfanilamide beneath the graft interfered in any way with the "take" of the graft.

The clinical value of this local chemotherapy at the time of operation is demonstrated by the fact that all complete failures, due to a streptococcal infection, were found to have not had this added protection or to have presented a sulfanilamide-resistant streptococcus, in which the drug had no effect

upon the organism. In five wounds, skin grafting was carried out successfully in the presence of hemolytic streptococci (Type-A), with the aid of local and oral chemotherapy. If, furthermore, one considers that 72 per cent (81 cases) of these granulating wounds were found to have been infected by hemolytic streptococci at some time in their clinical course, the importance of chemotherapy is evident (Table I). Oral sulfanilamide was administered in doses of from three to six grams daily, in the adult, over a period of from three to seven days in those patients whose wounds were recently freed of streptococci (24 cases). The percentage of skin graft "take" was no higher in those cases receiving oral chemotherapy.

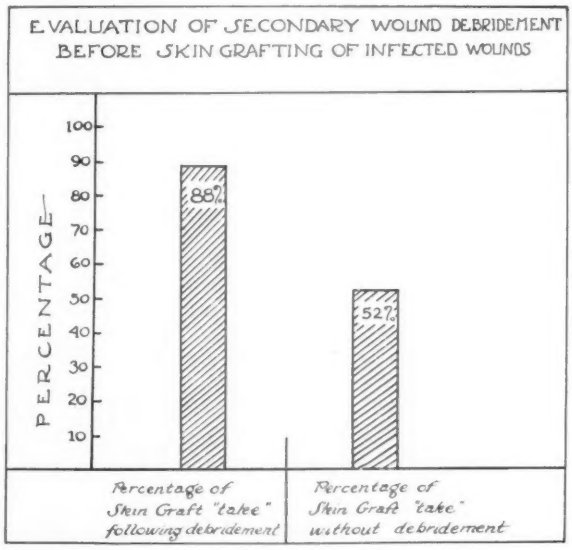


CHART 1.

The *Bacillus pyocyaneus* causes failure in most cases where skin grafting is attempted in its presence. Through, probably, a proteolytic action of the organism, the graft becomes very thick, greasy in appearance, and, finally, is removed as a slough. Practical failures were observed in the five cases grafted in the presence of *Bacillus pyocyaneus*. In five other cases grafting was performed after excision of the wound. In two cases, the graft was successful, and there was no reappearance of the organism. In three cases, grafting was nearly completely successful, although a recurrence of the *Bacillus pyocyaneus* was noted. These wounds healed rapidly by second intention. It seems to be a distinct advantage in wounds containing *Bacillus pyocyaneus* to perform excision before skin grafting, as this organism does not appear to thrive in freshly excised tissues. The influence of *Bacillus proteus* upon skin grafting was not observed.

The staphylococcus seems to influence the "take" of the skin graft only in proportion to the amount of exudate produced in the wound. Most cases

of complete "take" of grafts were noted to have presented staphylococci and diphtheroids at the time of operation. However, wound healing and, consequently, successful skin grafting does not depend totally upon the bacterial status of the wound. A wound may be sterile, but may present no evidence of healing.

(2) *Wound Fibrosis.*—The production of fibrous tissue in the deep layer of the granulation tissue of the wound diminishes the local blood supply and tends to create a poor base for a skin graft. It would seem preferable, therefore, particularly in older wounds, to excise the wound, whenever this is possible in order to obtain a vascular base for the graft.

Statistics showed (Chart I) that when secondary wound excision was done (54 cases) the percentage of skin graft "take" was 88 per cent. When wound excision was not done (56 cases) the percentage of skin graft "take" was 52 per cent. In some of the cases in this latter group (22 cases) the granulating layer was superficially excised or scraped, thus exposing the fibrous layer before grafting. In these cases the percentage of skin graft "take" was 68 per cent.

SECONDARY DÉBRIDEMENT (WOUND EXCISION)

Secondary débridement of unhealed wounds consists in excision of the whole wound. This includes the infected and fibrotic granulation tissue and the regenerated epithelium until normal appearing tissues are exposed (Fig. 4). After this procedure, the wound edges return to the position they occupied before contraction brought them closer together. The graft is applied upon this vascular muscle or fascia. The great objection to this type of procedure in an infected wound is the possibility of a flare-up of a quiescent infection, particularly streptococcal. It is felt that local chemotherapy as an adjunct to secondary débridement prevents such an occurrence. Complete secondary débridement, however, is not always feasible, particularly for anatomic reasons. Extensive wounds over important nerves or vessels, or close to a joint capsule cannot be resected without danger to these structures. If the wound is over bone, there should be no hesitancy in resecting the wound down to periosteum, as skin grafts "take" well on this vascular covering of bone.

TREATMENT WHERE SECONDARY DÉBRIDEMENT (WOUND EXCISION) IS IMPOSSIBLE

Where secondary débridement cannot be done it is necessary to produce, by other means, a wound devoid of suppuration and bring about good local circulation. Attempts are made to accomplish the following:

(1) *Elimination of Suppuration.*—Moist dressings, using a wide mesh vaselined gauze or a perforated nonadherent silk, will allow the continuous removal of purulent exudate. The chemotherapeutic effect of the sulfonamides can then take place without being inhibited by the presence of pus. Local chemotherapy is highly successful against the hemolytic streptococcus, and less successful against other infecting organisms such as *Bacillus pyo-*

cyaneus and the staphylococci. A 2 per cent solution of acetic acid has proven the best method of combating the *Bacillus pyocyaneus*. In a number of cases the application of sulfanilamide powder, four times daily, did rid the wound of this organism.

On dressings, it is important to treat the skin around the wound with as much care as the wound itself. Any small crust in the skin around the wound may hide a nest of organisms. Saline baths, either the total-bath around the part, particularly helpful in multiple wounds or the partial limb-bath, at temperatures varying from 98.6° to 110° F. prove extremely useful.

The Bunyan envelope applied to the extremity in bed, without the necessity of moving the patient is valuable,[3] particularly where other equipment is limited. A 5 per cent hypochlorite solution is used for irrigations. One disadvantage of the Bunyan envelope is the impossibility of applying the proper amount of pressure over the wound.

FIG. 4.—Illustrating secondary wound resection (débridement).

(2) *Provision of Good Local Circulation.*—Firm elastic pressure should be established during the intervals between the dressings or baths, not only over the wound itself, but over the whole of the extremity distal to the wound. The dependent position should be avoided and complete immobilization is essential.

When suppuration is controlled and a good bacterial status is obtained, the superficial layer of the granulations is resected down to the fibrous layer, and skin grafts are applied over a thin layer of sulfanilamide powder. Thus, by eliminating the pus-producing granulations, a greater chance of skin graft "take" is obtained than if the graft were applied to the untouched granulations.

The Choice of Sulfonamide for Local Chemotherapy in Skin Grafting.—Sulfanilamide and sulfathiazole were the only two compounds used. Sulfanilamide was preferred for local use in open wounds on account of its higher absorption rate. Sulfathiazole, unless insufflated in very small quantities, tended to "cake." This situation was particularly important under skin grafts. Skin grafts applied over sulfanilamide healed well; over sulfathiazole numerous small areas in the graft appeared to have broken down, possibly due to the unabsorbed sulfathiazole. Sulfathiazole was used, however, where a slow progressive absorption was desired as in a wound under closed plaster. In such cases the drug was found in the blood for as long as three weeks.[4]

Observations on Epithelization.—The "Closed Plaster" Versus The

"Open" Treatment of Wounds: Under plaster the wounds received complete immobilization and adequate pressure, which controlled systemic infection and favored local circulation.[5] Local infection was not controlled as evidenced by the purulent exudate containing a rich and varied bacterial flora.

The "closed plaster" appeared to favor, to a high degree, the connective tissue repair of the wound. It was a constant surprise at the change of plaster to see the vascular-appearing granulations under the pus. It did not, however, seem to favor epithelial regeneration, which was very slow. Some wounds, after months in plaster, showed little new epithelium. The epithelium, furthermore, appeared of poor quality, thin, and could easily be wiped away with gauze.

Generally speaking, the wounds that did heal well under plaster appeared to do so by maximal contraction and by minimal epithelization. It is felt that these facts are explained by the fact that the stagnation of purulent exudate is unfavorable to epithelial growth.

Attempts were made to dress the wounds of compound fractures through windows cut in the plaster. This method proved unsatisfactory. Local edema occurred in the wound, it was found difficult to keep the area surrounding the wound clean, and exudate tended to diffuse under the plaster. To expose the wound adequately it was often necessary to cut a window so large as to menace the stability of the fixation.

Wounds presenting skin losses were frequently observed under plaster where, because of their unfavorable anatomic position and the extent of the skin loss, epithelial healing could only take place, if at all, after a long time-interval. During this time the increasing fibrosis would be such as to seriously impair the circulation of the limb by constriction, and to produce wound healing of poor quality which is destined to break down repeatedly. Other cases were observed where unhealed superficial tissue losses under plaster held back the performance of important secondary surgery on the bones, the nerves or the tendons.

It became evident that in such cases great benefit would be derived from successful skin grafting of the wounds.

Secondary Skin Grafting in Compound Fractures.—In these cases, the wounds were observed when the plaster was changed and cultures were taken. If grafting of the wound appeared indicated, plans were made for this procedure at the next change of plaster. After removal of the plaster, the wound and surrounding skin were thoroughly washed, and all exudate, dried pus, and crusts were removed. A skin graft was then removed from one of the thighs. A total débridement of the wound was performed, in which all tissue down to healthy muscle, fascia or periosteum was removed. Sulfanilamide powder was then applied with Pearce's insufflator and the skin graft immobilized with a pressure dressing and bandage. A plaster encasement was reapplied to the extremity. On removal of the plaster from four to six weeks later, skin graft "takes," varying from 70 to 100 per cent were found (Fig. 5A and B). This type of procedure was carried out in 11

cases presenting extensive wounds in relation with compound fractures (Table II).

TABLE II

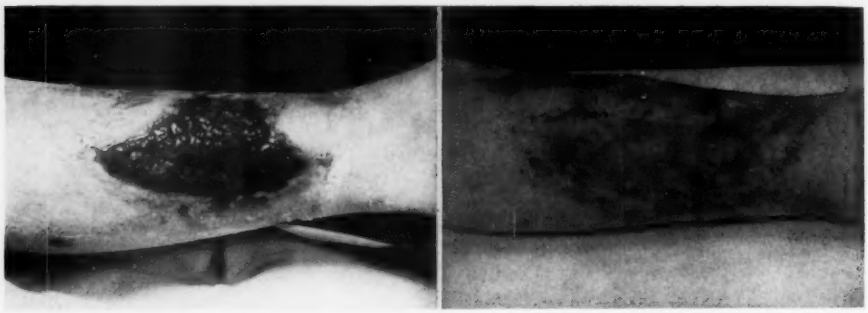
SKIN GRAFTING OF INFECTED WOUNDS OF COMPOUND FRACTURES

Case No.	Type and Cause of Injury	Primary Treatment	No. of Days between Injury and Skin Grafting	Secondary Débridement before Skin Grafting?	Bacteriology at Time of Skin Graft	Percentage of Skin Graft "Takes"
1.	Compound fracture of rt. tibia and fibula. (Motorcycle accident)	Débridement. Reduction. Sulfanilamide powder in wound. Closed plaster.	35 days	Yes. Wound of anterolateral aspect of leg. 8x9 cm.	*Staphylococcus aureus*	90
2.	Compound fracture rt. ulna and radius. (Bomb fragment)	Débridement. Reduction. No sulfanilamide powder in wound. Closed plaster.	91 days	Yes. Two wounds encircling forearm. 5x7 cm. each.	No growth on cultures.	100
3.	Compound fracture of tibia. (Tank crash)	Primary attempt at closure of defect by plastic, using two lateral flaps. Closed plaster.	37 days	Not done. Wound 10x15 cm.	Few *B. pyocyaneus*	0
4.	Same case as above.	Same treatment as above.	56 days	Yes. Same wound 10x15 cm.	Few *B. pyocyaneus*	80
5.	Compound fracture upper end rt. radius. (Bombing)	Débridement. Reduction. Closed plaster.	39 days	Yes. Upper lateral aspect of rt. forearm. 8x13 cm.	*Staphylococcus aureus* and *albus*	100
6.	Compound fracture upper ⅓ of tibia. (Motorcycle accident)	Treatment same as above.	Treated 8 months in closed plaster. Unhealed.	Yes. Superior anterolateral aspect rt. leg. 18x9 cm.	Few *Staph. aureus* and *B. pyocyaneus*	70
7.	Compound fracture tibia, fibula lower ⅓. (Motorcycle accident)	Treatment same as above.	32 days	Yes. Anterolateral aspect leg. 10x12 cm.	Hem. strep., *Staph. albus*	90
8.	Deep burns and fracture tibia and fibula. (Pt. pinned in bombed house by fallen masonry, burned by coals from fire.	Closed plaster, without débridement.	14 days	Yes. Removal plaster. Sec. débrid., two areas. 10x12 cm.	*Staph. aureus.* Diphtheroids.	85
9.	Fracture-dislocation head of radius. Open wound lft. elbow. (Crushing injury sustained in bombed house)	Resection head of radius. Débridement. Sulfanilamide powder. Closed plaster.	15 days	Yes. Saline soaks for 3 days; then skin grafting after conservative sec. débrid., removing sloughs. Sulf. powder. Left elbow. 26x15 cm.	Few hem. strep. Type-C., and few *B. pyocyaneus*	85
10.	Compound fracture rt. tibia and fibula, lower ⅓. (Motorcycle accident)	Same as above.	41 days	Yes. Anterolateral aspect of rt. leg; small area bone exposed. 10x13 cm.	Hem. strep., few *Staph. aureus* and diphtheroids.	100 except for area over bare bone.
11.	Compound fracture of left tibia and fibula. (Bombing)	Débridement. Reduction. Closed plaster.	22 days	Yes. Ant. aspect leg; skin grafting. Closed plaster. 6x9 cm.	Hem. strep.	70

This method of skin grafting wounds of compound fractures interferes in no way with the routine closed plaster treatment. It brings, however,

to this method of treatment, the one element in which it appears deficient, namely, epithelium.

Removal of Sloughs, Particularly in Burns.—Wounds that have not been primarily débrided often present large sloughs. These sloughs should be treated surgically by secondary débridement followed by immediate skin grafting. This situation is particularly frequent in severe burns where it is difficult to estimate, at the onset, how much tissue damage has taken place. If immobilized in plaster for ten days to two weeks the slough delimits itself and can be débrided and grafted at that time. This secondary débridement obviates the necessity of waiting for these sloughs to separate spontaneously. This may take weeks during which much time is lost, wound fibrosis is developing, and secondary infection may supervene.



A B

FIG. 5.—(A) Wound of compound fracture of tibia. (B) Appearance of wound after secondary débridement, skin grafting, and immobilization in plaster for four weeks. The skin grafting has been done during a change of plaster, thus interfering in no way with the routine closed plaster treatment of the fracture.

Secondary Skin Grafting in Compound Fractures Treated by External Skeletal Pin-Fixation, without Closed Plaster.—In such cases the wounds can be treated by local chemotherapy, and other methods, under conditions similar to those found in skin grafting of open granulating wounds as described above.

(1) *Primary Débridement: Primary Skin Grafting.*—The most opportune time to provide the wound with a skin covering would appear to be at the time of the primary débridement. After resection of all the devitalized tissue and removal of foreign bodies, thus, creating a saucer-shaped wound, a skin graft is laid into the wound and held in position by the firm even pressure produced by cotton-wool or sponge. The plaster can be applied immediately over this dressing or a bandage including not only the wound area but the whole limb can be used for fixation before the application of the plaster.

The compound fracture is then treated by the closed plaster method, the plaster being changed at the desired time-interval. The skin grafting has in no way interfered with the routine closed plaster treatment, but adds to this method the great advantage of an epithelized wound.

(2) *Secondary Débridement: Secondary Skin Grafting.*—Under the stress

of conditions prevailing at the time the patient is received at the hospital (air raid), in order to save time, it may be preferable to perform the primary débridement, use the local chemotherapy in the form of sulfanilamide powder or a gauze dressing saturated with the drug in the wound, then apply the plaster and postpone the skin grafting until more time is available. It is possible that the tenth day may be the most suitable time for this procedure. The plaster is then removed and a skin graft applied.

Often it is impossible in crushing injuries, or in deep burns, third degree, to distinguish the extent or the depth of the tissue destruction. This is particularly true in burns. In some burns, it is true, the white, dead parchment skin is obviously destroyed; nor can there be any doubt when there is marked charring of the tissue. A primary débridement followed by a primary skin graft constitutes the treatment of choice. If there is doubt, however, as to the extent or the depth of the burn, the extremity can be immobilized in a skin-tight plaster. This gives the injured extremity rest and adequate pressure, and the plaster protects the wound against cross-infection. This plaster immobilization is carried out for ten to 15 days. At this time a slough will have appeared, delimiting the area of devitalized skin and superficial tissue. The plaster is removed, a secondary débridement is carried out, and is followed by an immediate skin grafting procedure.

Contraindications for Skin Grafting.—It is evident in many cases where the wound is deep, involving the fascial planes; where suppuration exists; or where there may be a large muscle tissue defect—that it is essential to wait until infection is limited and the connective tissue repair has taken place before skin grafting can be considered.

Types of Skin Graft Used.—The most suitable graft is the "thick, razor-graft," also called the "intermediate" or "split-graft." It is cut with the Blair skin graft knife, usually from the lateral or medial aspects of the thigh. This graft is thicker than the Ollier-Thiersch. The latter graft, because of its thinness, has a slightly higher degree of "take." It is, however, less resistant to functional stress than the intermediate graft which gives a strong epithelial covering that in most cases will be permanent.

The "pinch-graft" (Davis) is not suitable in the type of repair considered. It gives epithelization by "second intention," the epithelium spreads out from the individual islands that are grafted. The "pinch-graft" is valuable in extensive burns, if little skin is available for skin grafting, otherwise the best result can be obtained with the "sheet" type of graft, which, if placed under suitable conditions, will take *per primam*.

Removal of the razor-graft requires some practiced skill. Two recent additions to the surgeon's armamentarium have rendered the removal of skin grafts easier, namely, the dermatome (Padgett), and the calibrated razor knife (Humby). The thickness of the graft should be about 14/1000 of an inch, as calibrated by the Padgett dermatome. The graft can be spread over tullegras or vaselined gauze (Gillies) before being applied over the

wound. If multiple pieces of graft are needed they are laid on the tullegras slightly overlapping, so as to form a continuous epithelial covering.

Covering of Bone and Tendon.—Skin grafts are not successful over bone deprived of periosteum. Although they will take well on the latter membrane, they are usually unsuccessful over tendon deprived of its sheath. In such cases it is necessary to cover exposed structures with a flap of skin consisting of subcutaneous tissue and fat, cut from the side of the extremity and transposed over the defect. The wider this flap is made, the better its blood supply.

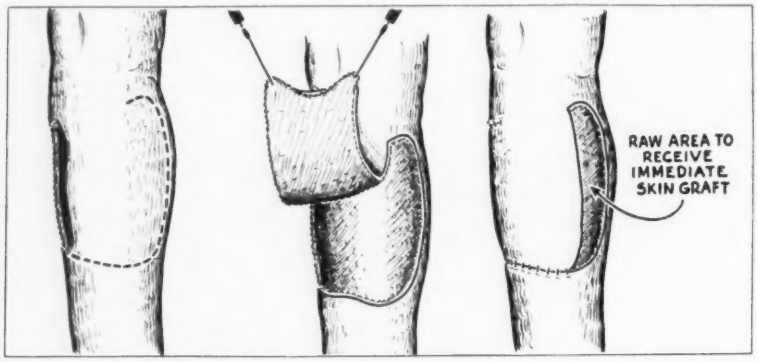


FIG. 6.—Rotation flap for covering tibial graft. (A) Outline of rotation flap. (B) Rotation flap is undermined and elevated. (C) Rotation of flap is completed and flap covers the tibial defect.

In the tibial region the use of local flaps will often allow covering the bare bone. A rotation-flap (Fig. 6) is suggested as the best type of flap, particularly in long defects. Here, the use of parallel advancement-flaps may be dangerous, as they tend to become devitalized because of their length. Over the dorsum of the foot, if there is a large defect, local flaps are not available. The employment of an immediate direct flap from the opposite thigh is rarely feasible on account of the difficult position of immobilization necessitated in a patient who is often in poor condition. In such cases the removal of the outer table of bone will favor the growth of granulation tissue under a closed plaster. On these granulations a skin graft may be applied as a temporary dressing. Often this skin graft may not stand the strain of walking, or the pressure of the shoe. The skin graft can then be excised and a full-thickness flap of skin be applied, taken from the opposite leg.

The immediate covering of tendon is imperative to prevent sloughing. In small defects of the finger the procedure is employed in which a flap is taken from the side of the finger and used to cover the tendon. Then the defect left by the mobilization of this flap is skin-grafted. In large defects, where the tendon is uncovered over the whole length of the finger, the digit must be covered by an immediate direct flap, or buried in a skin-pocket in the abdomen or thigh.

Avulsed Flaps.—Large avulsed flaps, when they present a wide base, may be successfully sutured back into position. If the base appears insufficient it

is preferable to remove all the fat, until the base of chorium is exposed, thus converting it into a full-thickness graft over which adequate pressure is applied as for a free graft.

SUMMARY AND CONCLUSIONS

War wounds with extensive skin loss are often followed by contractions, constrictions and deformities of the extremities, necessitating secondary reconstructive surgery. In wounds remaining unepithelized longer than from three to five weeks, fibrous tissue changes occur which diminish local blood supply and open the way to secondary infection.

Skin grafting of infected granulating wounds, following secondary débridement and local use of sulfanilamide powder has given success in percentage of skin graft "takes," estimated at 88 per cent in 56 cases. In wounds of compound fractures, skin grafting has been undertaken successfully during the routine change of the closed plaster following secondary débridement and local use of sulfanilamide powder.

War wounds presenting skin losses should be skin-grafted immediately by a primary "skin dressing." This procedure avoids complications and greatly reduces the healing period of the wound.

When immediate skin grafting is not possible or when it is impossible to determine exactly the extent of the tissue destruction, as in deep burns, immobilization in plaster for ten days to two weeks allows the devitalized tissue to delimit itself in a slough, which is then resected and skin-grafted.

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BRAIN ABSCESS OF UNCOMMON ORIGIN — RELATION TO OSTEOMYELITIS OF THE SKULL *

A CLINICOPATHOLOGIC STUDY

VICTOR W. EISENSTEIN, M.D.,
PITTSBURGH, PA.
E. D. FRIEDMAN, M.D.,
AND
CHARLES DAVISON, M.D.
NEW YORK, N. Y.

FROM THE NEUROLOGIC AND NEUROPATHOLOGIC DIVISIONS OF THE MONTEFIORE AND BETH ISRAEL HOSPITALS, AND THE DEPARTMENT OF NEUROLOGY, NEW YORK UNIVERSITY COLLEGE OF MEDICINE, NEW YORK, N. Y.

APPROXIMATELY two-thirds of all brain abscesses arise from local infections about the head.[1] While most are of otitic origin, about 10 per cent of the total number arise from other foci about the cranium,[1, 3] notably the frontal sinuses and the soft tissues of the face and scalp. To the latter groups, osteomyelitis of the skull bears close relationship, inasmuch as it is often the first complication to arise from the original site of infection. It, therefore, appears desirable, in the interest of prophylaxis, to study the mechanism whereby a simple local infection about the head leads to cranial, then graver intracranial involvement.

Swimming,[4, 5, 6, 7, 8] and the aspiration of water into the nose, has been the frequent origin of a fulminating infection which led to osteomyelitis, brain abscess, and death, particularly in young individuals, as illustrated in one of our cases. Other common conditions that have preceded such involvement are the ordinary cold and its accessory sinusitis,[9, 10, 11] furunculosis of the face and scalp,[5, 12] peritonsillar abscesses,[13, 13a] and apparently minor head injuries.[2a, 14, 15] Simple "office treatments" of the nose and accessory sinuses[16] have likewise been the precursors of intracranial infection, though not as commonly as have radical sinus operations.[16, 17, 18]

The importance of uncommon local foci as causes of cerebral abscess has recently been recognized by Carmichael, Kernohan, and Adson,[27] who indicated that, aside from isolated case reports, adequate statistics on this group are wanting. The relative incidence of cerebral abscesses of various origins among autopsied cases recently reported may be seen from Table I.

In a recent review, Mosher[4] pointed out that fully half of the cases of spreading osteomyelitis of the skull are complicated by intracranial abscesses. Of 91 cases of cranial osteomyelitis reported by Lemon,[9] brain abscess was found as a complication in only 30 per cent. In Turner and Reynolds'[11] series of intracranial pyogenic diseases there were four brain abscesses, all associated with bony involvement. In McKenzie's[21] series of 48 cases of

* Read at the Combined Meeting of the New York Neurologic Society and Section of Neurology and Psychiatry of the New York Academy of Medicine, May 6, 1941.

TABLE I

COMPARATIVE INCIDENCE OF BRAIN ABSCESSES OF VARIOUS ORIGINS

Report of:	Total No. of Cases of Brain Abscess	No. Cases of Otitic Origin	No. Cases of Rhinogenic Origin	No. Cases Due to Other Local Causes	Remarks
Evans[1]	194	109	12	8	Found among 14,543 autopsied cases
Courville and Rosenvald[2]	52	47	7		Found among 15,000 autopsied cases
Eggston[20]	67	37	18	3	Of the last group, all followed osteomyelitis of the skull
Bonninghaus[3]	713	631	82		Cases collected from the literature up to 1910
Mayfield and Spurling[19]	52	16	6	7	Based upon a study of 32 patients surgically treated

rhinogenic osteomyelitis of the skull, 45 had followed frontal sinus disease, and brain abscess had developed in ten. The diffuse form of osteomyelitis has been found most frequently in connection with paranasal sinus infections; the more localized forms generally as a complication of local trauma or infection. Microscopic foci of osteomyelitis have been demonstrated about infected nasal sinuses by Kramer and Som.[36] While diffuse osteomyelitis is uncommon after ear and mastoid disease, minute foci of involvement of the petrous tip have recently been revealed as real or potential causes of brain abscess (Kopetzky and Almour,[22] Eagleton,[23] and Fowler[24]). In our consideration of the pathogenesis of brain abscess, the importance of the intermediate rôle of osteomyelitis in relation to brain abscess will be considered and the therapeutic implications noted.

REPORT OF CASES

Case 1.—M. K., male, age 45, was admitted to Beth Israel Hospital, August 16, 1938, complaining of severe sore throat. Examination revealed edema of the pillars and soft palate, and a necrotic grayish patch behind the left posterior pillar.

Neurologic Examination.—The patient appeared dull, and presented markedly defective speech and diminution of vision in the right eye. Horizontal nystagmus was present bilaterally. The pupils reacted well and the fundi showed a slight temporal pallor of the disks, but no swelling. There was slight paresis of the lower facial muscles. Ataxia was present in the right finger-to-nose test. All of the deep reflexes were normal and there were no pathologic reflexes.

Course.—Excruciating headache developed, which was resistant to all forms of therapy. Hearing became markedly impaired bilaterally, and bone exceeded air conduction, but the ear drums were of normal appearance. The ocular fundi showed some fullness of the veins and some blurring of the nasal side of the disks. While the first four weeks of the illness were marked by an afebrile course, the last week was marked by a sudden and persistent elevation of temperature of 103° to 105° F. The pulse rate was coincidentally elevated. In spite of the administration of large doses of sulfanilamide and repeated spinal taps, the patient died 39 days after admission.

Laboratory Data.—R.B.C. 4,500,000; Hb. 80 per cent; W.B.C. 9,500, with 75 per cent polymorphonuclear leukocytes, 22 mononuclear cells and five eosinophils. Roentgenologic examinations of the skull were negative.

Spinal fluid, examined September 14, 1938, was clear, under 85 Mm. of water pressure, contained 60 mg. per cent of protein, 580 mg. per cent of chlorides, and 36 mg.

per cent of glucose. The cell count revealed eight white blood cells, of which four were polymorphonuclear leukocytes. The smear showed no organisms, and the culture was sterile.

Autopsy.—Examination disclosed the presence of a retropharyngeal abscess, with extension of the inflammatory process in the epipharyngeal tissues (Fig. 1); osteomyelitis of the clivus (Fig. 2). The bony tissue at the base of the skull was partially destroyed. Streaks of thick yellowish-green exudate were noted in the meninges in the region of the cisterna magna and over the right cerebellar hemisphere.

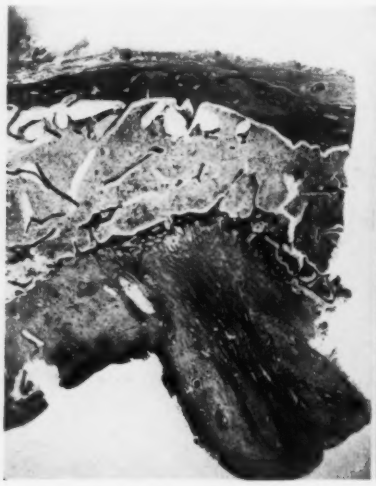

FIG. 1.—Case 1: Base of the skull showing swollen epipharynx with inflammatory changes. The marrow spaces are between the epipharynx and the bony tissue.

FIG. 2.—Case 1: Inflammatory process in tissues adjoining the base of the skull. Note the destruction of bone.

Microscopic Examination.—Sections of bone removed from the clivus by a Harke incision showed hemorrhage and granulation tissue, with destruction of bone (Fig. 2). The connective tissue between the pharynx and bone was widely infiltrated with leukocytes (Fig. 2).

The meninges were slightly thickened and were infiltrated by lymphocytes, plasma, endothelial cells and a few macrophages. The vessels of the first layer of the cortex were invaded by the same type of inflammatory cells. The nerve cells appeared normal except for occasional ischemia and slight loss in chromatin. There was slight proliferation of the endothelium of the smaller cortical vessels.

Sections through the centrum ovale disclosed inflammatory foci. The basal meninges and the meninges in the region of the insula and those of the cerebellum and the spinal cord showed the same type of inflammatory reaction as described above. The third ventricle contained inflammatory cells. The ependyma was slightly thickened. Ischemia and other cell changes were noted throughout the thalamus.

Comment.—This case illustrates the advance of a peritonsillar abscess to meningitis and abortive abscess formation in the brain. The intermediate relationship of osteomyelitis at the base of the skull was suspected in this instance. A careful search through the Harke incision, on postmortem examination, revealed the presence of a minute focus of osteomyelitis in the clivus (Fig. 2*).

*We are indebted to Dr. A. Plaut, pathologist of Beth Israel Hospital, for the studies of the bone specimens in the above case.

Case 2.—A. W., male, age 28, was admitted to Sydenham Hospital, March 5, 1938. For the previous two weeks he had suffered from sore throat, difficulty in swallowing and some fever. There was a fluctuant mass in the pharynx which was incised and drained of pus. The temperature rose to 106° F., and the patient appeared lethargic.

Neurologic Examination.—The patient was aphasic but responded to commands made as gestures. There was neck rigidity and a bilateral Kernig sign. The right cheek puffed out with each respiration. The right corneal reflex was diminished. All of the deep tendon reflexes were absent. There was no Babinski sign. Sensory examination was normal.

FIG. 3 A.

FIG. 3 B.

FIG. 3 A.—Case 3: Scar and abscess over the right frontal, premotor and motor convolutions.
FIG. 3 B.—Case 3: Subarachnoid hemorrhage extending from the frontal to the occipital convolutions.

Laboratory Data.—R.B.C. 4,590,000; W.B.C. 27,000, with 85 per cent polymorphonuclear leukocytes. Pus obtained from the abscess in the pharynx yielded streptococcus nonhemolyticus on culture. The blood cultures were sterile throughout the illness. The spinal fluid was under increased pressure and contained 300 cells per cu. Mm., predominantly polymorphonuclear leukocytes.

Autopsy.—Gross examination revealed a parapharyngeal abscess; empyema of the sphenoid sinus; empyema of the left transverse, cavernous, and superior petrosal sinuses of the dura; purulent meningo-encephalitis of the temporal, parietal, and frontal lobes of the brain; multiple brain abscesses of the left cerebral hemisphere and a solitary abscess of the vermis cerebelli. The microscopic examination of the brain abscesses was not different from those described in the other cases.

Comment.—Brain abscesses following peritonsillar abscesses are of extremely rare occurrence. Two similar cases have been reported within the past ten years.[13, 13a] The mechanism of spread has been illustrated in Case 1.

Case 3.—R. L., female, age 48, was admitted to the Montefiore Hospital, November 24, 1926. An abortion performed 18 years previously had been complicated by pelvic peritonitis, and for 15 years thereafter was followed by multiple abscesses in various regions of the body. A large abscess had formed in the right temple, close to the eye, and had been incised and drained. Operation, in June, 1925, disclosed osteomyelitis of the skull about the outer angle of the orbit. Subsequently she developed headaches, recurrent attacks of vomiting, and pronounced exophthalmos of the right eye.

FIG. 4.—Case 3: Abscess destroying frontal and temporal convolutions, invading the basal ganglia. (myelin sheath stain)

In May, 1926, she lost consciousness for a few minutes. Examination disclosed weakness of the left hand, ataxia of the left upper extremity with slightly increased deep reflexes on the left. A craniotomy performed at this time revealed an extradural collection of pus and an abscess in the right frontal lobe of the brain. Subsequently flaccid left hemiplegia, hemihypalgesia, hemihypesthesia and hypthermesthesia, a Babinski sign, and convulsive episodes developed. On November 23, 1928 she became confused, apprehensive and incontinent, and died suddenly.

Autopsy.—The dura was adherent to the skull at the right temporal region by thin fibrous adhesions, and to the brain over the right frontal, precentral, and central convolutions by dense fibrous tags (Fig. 3 A). The right hemisphere was smaller than the left. On the left side, there was an extensive subarachnoid hemorrhage extending from the precentral convolution to the occipital lobe (Fig. 3 B), involving chiefly the superficial branches of the middle cerebral artery. An abscess measuring 2x2 cm. was present in the right temporal lobe. In some areas this mass showed signs of organization (Fig. 4). The structures adjacent to it (external capsule, internal capsule, caudate nucleus)

were partially invaded, distended, and destroyed (Fig. 4). Caudally the thalamus and the lenticular nuclei were compressed and their outlines were indistinct.

Microscopic Examination.—Myelin sheath preparations showed demyelination of the white fibers of the cortex, internal capsule, and basal ganglia (Fig. 4). In the van Gieson and cresyl violet stains, the abscess did not have a well-defined capsule, but disclosed numerous bands of connective tissue traversing it (Fig. 5). Between the dense mass of connective tissue and the damaged brain tissue there was a thin inner cellular zone consisting of lymphocytes, plasma, and endothelial cells. The brain tissue beyond this area consisted mainly of large collections of inflammatory cells, gitter cells, and congested blood vessels. The blood vessels, in the vicinity of the drained abscess and distant from it, showed extensive proliferative changes (Fig. 6 A). The perivascular spaces of some vessels

FIG. 5.—Case 3: The abscess does not have a well-defined capsule. Notice the bands of connective tissue traversing it. (van Gieson stain)

were infiltrated with inflammatory cells (Fig. 6 B); in others, all the coats were infiltrated with lymphocytes, plasma, endothelial and compound granular corpuscles (Fig. 6 A).

The involved cortical convolutions disclosed a complete distortion in the arrangement of the cyto-architectural layers with marked destructive changes in the nerve and glia cells and proliferation of the vessels. The ganglion cells in the cortex adjacent or distal to the abscess had also undergone various pathologic changes from mild chromatolysis, swelling, and ischemia to complete neuronophagia and severe cell changes of Nissl. The subarachnoid spaces near and distal from the abscess were distended and filled with red blood cells, lymphocytes, plasma, endothelial and gitter cells.

Comment.—In this case the brain abscess followed osteomyelitis of the frontal bone in the region of the anterior temporal diploic vein. The original focus of scalp infection was probably initiated by pyemia following an abortion, and extending over a period of 15 years.

Case 4.—J. W., male, age 12, was admitted to the Montefiore Hospital, May 1, 1936, with a history of acne and recurrent boils on the neck since January, 1936. A deep abscess had developed in the left side of the scalp, in the preauricular region, and had

been incised by the family physician. In March, 1936, the patient experienced repeated twitchings in the right arm.

Neurologic Examination.—This disclosed slight motor weakness, increased reflexes and a Babinski sign on the right side. There were no sensory changes. The disk margins were slightly blurred. The visual fields and acuity were normal.

Course.—A low-grade temperature, occipital headaches, and numerous right-sided jacksonian seizures persisted. The papilledema increased. An encephalogram, performed

FIG. 6 A.

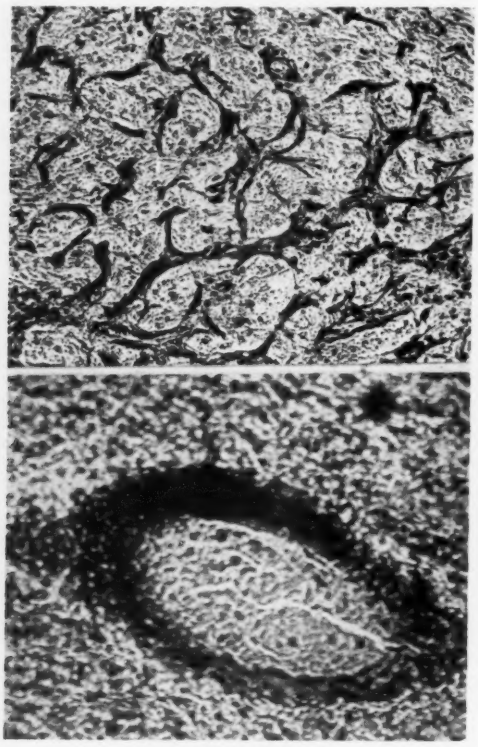

FIG. 6 B.

FIG. 6 A.—Case 3: Proliferation of the vessels in the region of the abscess. (van Gieson stain)

FIG. 6 B.—Case 3: Perivascular infiltration as well as infiltration of all the coats of the vessels.

April 2, 1936, revealed distention and displacement downward of the left lateral ventricle. Exploration for brain abscess over the region suspected was negative. Following this, the patient became disoriented and developed sensory and motor aphasia and a right hemihypesthesia. On May 6, 1936, meningeal signs were observed. On reexploration a cerebral abscess was evacuated at the site of the original operation. The patient died the following day.

Laboratory Data.—Spinal fluid taken at the onset of patient's illness (March, 1936) was clear, but under pressure of 230 Mm. of water. It contained 110 cells; 56 per cent polymorphonuclear leukocytes, 44 per cent mononuclear cells. The total protein was 102 mg. per cent; sugar 44 mg. per cent; and chlorides 522 mg. per cent. A spinal tap taken prior to his final operation was under 310 Mm. of water pressure, appeared

turbid and contained 2,000 cells. Culture from the fluid contained the *Staphylococcus aureus* and a gram-positive bacillus.

Autopsy.—There was a left temporoparietal decompression with a cerebral hernia and adhesions around it. An extensive subarachnoid hemorrhage mixed with greenish, purulent exudate filled the basal, pontine, interpeduncular and interchiasmatic cisternae. On incising the splenium of the corpus callosum, purulent fluid escaped from the third ventricle. The greatest part of the white matter of the left hemisphere was destroyed and filled by mucopurulent material (Fig. 7).

Microscopic Examination.—Coronal sections through the striatum disclosed an area of excavation involving the greatest part of the centrum ovale and part of the white and gray matter. The left gyrus cingulus and the first frontal convolution contained

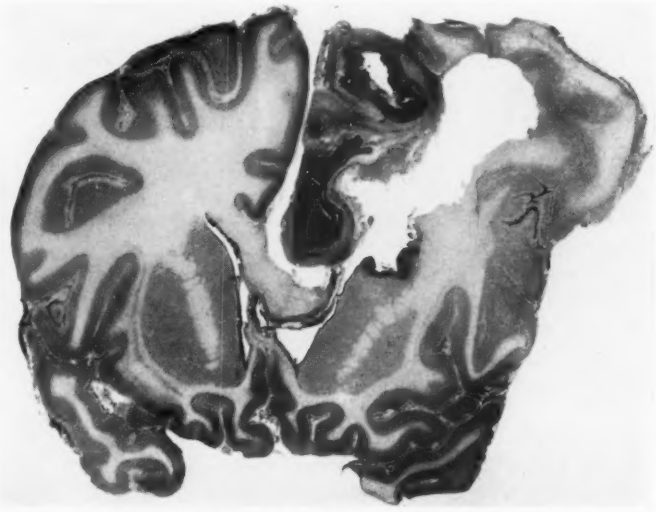

FIG. 7.—Case 4: Notice the two abscesses and the various zones in the left frontal and cingulus gyri; the marked area of destruction in the white matter and the ventricular infiltration by inflammatory cells.

two separate abscesses (Fig. 7). The cavity of the abscesses was surrounded by a dense zone of inflammatory cells, polymorphonuclear leukocytes, lymphocytes, plasma and endothelial cells, and necrotic material (Fig. 7). Next to this was a zone less dense consisting of necrotic material and some inflammatory cells (Fig. 7). Adjacent to this, there was another dense zone consisting of proliferating vessels, compound granular corpuscles, inflammatory cells, fibroblasts, perivascular infiltrations, and microglia cells (Fig. 7). Beyond this zone, there were miliary abscesses, dense areas of inflammatory cells, and occasional proliferating vessels. The adjacent cortical convolutions showed a marked distortion in the arrangement of the cyto-architectural layers and perivascular infiltrations. The nerve and glia cells showed all types of pathologic changes. In some areas there were also numerous *gemästete* glia cells. The meninges were thickened and invaded by the same type of cells as seen in the region of the abscess.

Comment.—This case again illustrates the extension of a pathologic process from an infection of the scalp into the bones of the skull and the brain, leading to abscess formation.

Case 5.—J. K., male, age 11, was admitted to the Montefiore Hospital, Pittsburgh, Pa., July 4, 1933. While swimming, he had aspirated water into his nostrils. Three days

later he was stricken with malaise, fever, and vomiting, and complained of sharp pain over the right upper eyelid, which was swollen and tender.

Roentgenologic examination, July 5, 1933, revealed marked cloudiness of the right antrum, frontal, ethmoidal, and sphenoidal sinuses. The right antrum was punctured and drained of pus which yielded *Staphylococcus aureus*.

On the fourth day after admission the entire forehead appeared swollen and red, and both eyelids were pasted shut. The swelling gradually receded, but left, in its wake, two localized fluctuating masses (pericranial abscesses). Incision and drainage of these areas was followed by a chill; nevertheless, clinical improvement ensued, and the temperature dropped to normal levels. During the following week, several more doughy, fluctuating areas, about the size of walnuts, appeared on the scalp in the temporal regions. Roentgenologic examination failed to reveal the presence of bone destruction at this time.

During the third week the patient vomited and complained of dull, diffuse, headache and papilledema was observed. Later, periods of stupor, twitching of the right side of the face, and clonic contractions of the right arm and leg appeared. The left pupil was larger than the right; both reacted sluggishly to light. Hyperreflexia, marked ankle clonus, and sensory impairment were present on the right side for several days. Aphasia was also present.

Laboratory Data.—R.B.C. normal. W.B.C. 16,300, with 82 per cent polymorphonuclear leukocytes. Blood cultures were sterile. The spinal puncture yielded a clear fluid, containing 13 cells per cu. Mm., of which three were polymorphonuclear neutrophils, and ten lymphocytes. Pandy's test was positive for globulin.

Course.—During the fifth week of the illness there was a sharp rise in temperature to 104° F., with chills, followed by the localization of another pericranial abscess. A probe passed into a discharging area encountered roughened bone which imparted a feeling like that of rotted wood. Roentgenograms at this time revealed a diffuse destructive process involving both tables and diploe of the frontal and parietal bones (Fig. 8). Ocular examination revealed reduction of central vision to 6/12, marked papilledema, enlarged blind spots, and contraction of fields in all meridians.

Despite the extensive suppurative bony involvement and the changes indicative of increased intracranial pressure, the patient continued to improve clinically and was walking about comfortably in the seventh week of his illness. He underwent an extensive sequestrectomy at the Mayo Clinic in October, 1933, and died on that day.

Autopsy.—Dr. A. W. Adson reported the finding of a diffuse osteomyelitis of the frontal and parietal bones of the skull, and the presence of a beginning abscess in the left temporal lobe of the brain.

Comment.—This case illustrates the typical march of events when paranasal infection, contracted after swimming, progressed to cranial osteomyelitis and brain abscess. The diagnosis of bony infection was obvious in the second week of his illness from the occurrence of Pott's puffy tumors of the forehead. At this time the disease was quiescent and the temperature normal. In the light of the present knowledge, it is felt that early and radical surgical therapy of osteomyelitis might have prevented the fatal intracranial complication.

Case 6.—H. J., male, age 13, was admitted to the service of Dr. S. J. Kopetzky at Beth Israel Hospital, November 24, 1934. A week prior to admission, he had taken ill with a cold, nasal discharge, and temperature of 102° F. Two days before admission, he developed pain above the right eye.

Examination revealed the presence of a thick, purulent discharge in the right nostril and edema about the right eye. On November 26, 1934, the right antrum was punctured. Several days later, the patient developed a chill and severe headache.

Neurologic Examination.—One week after admission nuchal rigidity and positive Kernig signs were present. The knee jerks were diminished, but the ankle jerks were active, with a tendency to clonus bilaterally. The abdominal reflexes were present bilaterally. There was no Babinski sign.

Laboratory Data.—Roentgenologic examination of the sinuses upon admission revealed evidence of right maxillary sinusitis. R.B.C. and urine showed no abnormality. W.B.C. 15,000, with 74 per cent polymorphonuclears. Two blood cultures taken during the course of the illness showed no growth. The spinal fluid, December 5, 1934, appeared cloudy, was under pressure of 125 Mm., and contained 2,600 cells per cu. Mm., predominantly polymorphonuclears.

Autopsy.—A thick, turbid exudate was present under the roof and along the inner wall of the right orbit. Microscopic examination revealed the thickening in the orbital

FIG. 8.—Case 5: Roentgenogram of skull showing destruction of bone as result of osteomyelitis of the frontoparietal region.

roof to consist of old and young osteophytes. The section also showed an area of bone necrosis.

Brain: The dura mater was adherent to the parietal bones. The leptomeninges were tense. The base of the brain, notably in the region of the chiasm, and the cavernous sinus were occupied by a turbid, brownish-green exudate. The left frontal lobe was softened and contained a deep-seated, well-encapsulated abscess 4x2.5x3 cm.

Case 7.—S. K., female, age 14, was admitted to the Beth Israel Hospital, February 27, 1935. At the age of three she had undergone a bilateral mastoidectomy and had remained well since. Ten days before admission, a reddened, swollen area had appeared about the old mastoid scar which had been incised by the family physician. Two days later, she developed repeated chills, septic elevations of temperature, and recurring vomiting.

The patient appeared drowsy, complained of diplopia and of burning in the left eye. A positive Kernig sign was present bilaterally. Some weakness was apparent in the left internal rectus muscle. W.B.C. 24,000, with 88 per cent polymorphonuclears. Roentgenologic examination of the skull revealed an area of decalcification in the wall of the left lateral sinus.

The left mastoid region was reexplored, February 28, 1935, and the left lateral

sinus was found exposed because of erosion of the surrounding bone. Postoperatively, the temperature dropped for a few days but the patient became drowsier and complained of pain across the bridge of the nose, radiating down the left cheek. The left pupil was larger than the right; there was drooping of the left upper eyelid, weakness of the left external rectus muscle, and lateral nystagmus. The left corneal reflex was absent. Reoperation, March 8, 1935, disclosed a thrombosis of the lateral sinus. The internal jugular vein was then ligated.

Course.—On April 1, 1935, a transitory sensory aphasia suddenly developed and lasted two days. A few days later a series of right jacksonian seizures occurred, lasted four hours, and were accompanied by clouding of consciousness, right hemiplegia, and signs of early papilledema. This episode cleared up within a few days but euphoria and facetiousness appeared. On April 12, 1935, papilledema and hemorrhages of both fundi, and gradual shrinking of the peripheral fields of vision were observed. Right facial weakness of the pseudoperipheral type, anomia, and alexia were present.

FIG. 9.—Case 7: Cavitations and brain abscesses in the frontal, motor and parietal regions. (cresyl violet stain)

On May 5, 1935, the patient became very drowsy, vomited repeatedly and lapsed into coma. The pulse rate fell to 55 per minute. Surgical reexploration disclosed a large abscess lying very deep in the left temporo-parietal region. The patient died three weeks later.

Laboratory Data.—Blood cultures taken on March 2 and 11, 1935, showed no bacterial growth. Spinal fluid, March 7, 1935, was clear, under a pressure of 90 Mm. of water; showed a trace of albumin, and 30 cells per cu. Mm., of which 22 were polymorphonuclears. No organisms were found on smear or culture.

Autopsy.—Examination of the cranial contents revealed the presence of osteomyelitis of the left temporal and petrous bones. The dura mater anterior to the crista galli contained many small grayish-white and yellowish blebs. A similar bleb was situated in the dura mater over the left petrous bone, but showed no perforations. The posterior half of the left lateral sinus contained thrombotic material. The sphenoid sinus was filled with mucopurulent material.

Brain: A large abscess was present in the left temporoparietal region and in part of the basal ganglia. The ependyma of the fourth ventricle was markedly thickened and contained mucopurulent collections.

Microscopic Examination.—In a horizontal section through the left hemisphere there were four large cavities (Fig. 9), situated in the frontal, motor, and parietal convolutions, involving both gray and white matter. In the cresyl violet preparation, the cavities were lined by an inner pale area surrounded by a more deeply stained zone (Fig.

9). The inner pale layer was made up of red blood cells, polymorphonuclear leukocytes, lymphocytes, plasma and endothelial cells. The deeper area consisted of numerous vessels surrounded by inflammatory cells and compound granular corpuscles. The coats of some of the vessels were completely infiltrated by the same type of cells. The meninges throughout the central nervous system were thickened and infiltrated with inflammatory cells.

Comment.—This case illustrates the rôle of osteomyelitis of the temporal bone as a precursor of brain abscess. The venous sinuses, explored shortly after the original bone infection, were thrombotic and indicated the venous pathway of intracranial invasion.

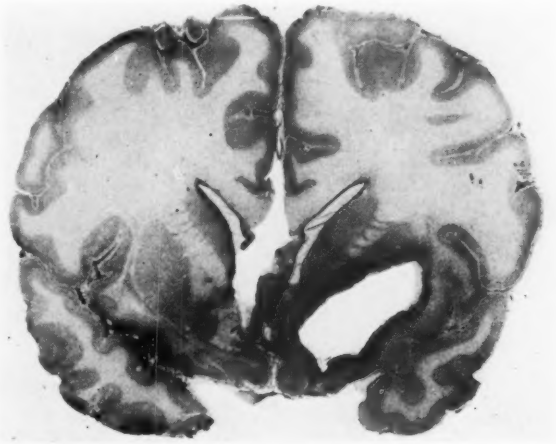

FIG. 10.—Case 8: Brain abscess of the right orbital convolution and part of the putamen. (cresyl violet stain)

Case 8.—C. S., male, age 23, was admitted to Beth Israel Hospital, February 27, 1939, with the history of an upper respiratory infection, sore throat, and pain over the right eye and nose since February 10, 1939. Examination disclosed obstruction of the right nasal passage, swollen turbinates, and a mucopurulent discharge from the right side of the nose.

Course.—Shortly after admission, the temperature became elevated and nuchal rigidity developed. The left pupil reacted sluggishly to light; the left palpebral fissure was widened, and there was slight weakness of the left facial musculature. Blurring of the left disk and bilateral Babinski signs appeared. The patient became drowsy and suffered from projectile vomiting. The spinal fluid contained 200 cells per cu. Mm.; 58 per cent polymorphonuclear leukocytes; total protein 67.5 mg.; glucose 41 mg. per cent. Ventriculography, performed March 23, 1939, disclosed evidence of a deep frontotemporal lesion close to the midline. The patient was operated upon, and greenish-yellow pus was removed. Subsequently right hemiplegia developed. The patient became stuporous and expired April 6, 1939.

Autopsy.—There was an abscess involving the white and gray matter of the second and third frontal convolutions. Another abscess was found in the right orbital convolutions (Fig. 10). The right ventricle was slightly constricted. The greatest part of the right pallidum and part of the white matter were replaced by an abscess which appeared encapsulated.

Microscopic Examination.—Complete coronal sections through the striatum disclosed an abscess involving the putamen and the greatest portion of the white and part

of the gray matter of the orbital convolutions (Fig. 10). Under high power, the myelin and axis cylinders surrounding the abscess showed all types of pathologic changes such as disintegration, swelling, or complete destruction. In the cresyl violet preparation, the abscess wall was found to consist of various layers: an inner lighter area formed by a layer of polymorphonuclear leukocytes (Fig. 11 A); next to it a zone which stained more deeply and consisted of proliferating vessels with perivascular infiltrates (Fig. 11 A and B). Next to this deeper layer, there was an outer zone which stained less deeply and which contained practically the same type of cells and numerous *gemästete* glia cells (Fig. 11 A). In this layer, there were also numerous vessels with extensive perivascular infiltration containing cells ten to 12 layers deep (Fig. 11 B). There was an increase in the microglia cells. At points distant to the abscess, perivascular infiltrations were noted.

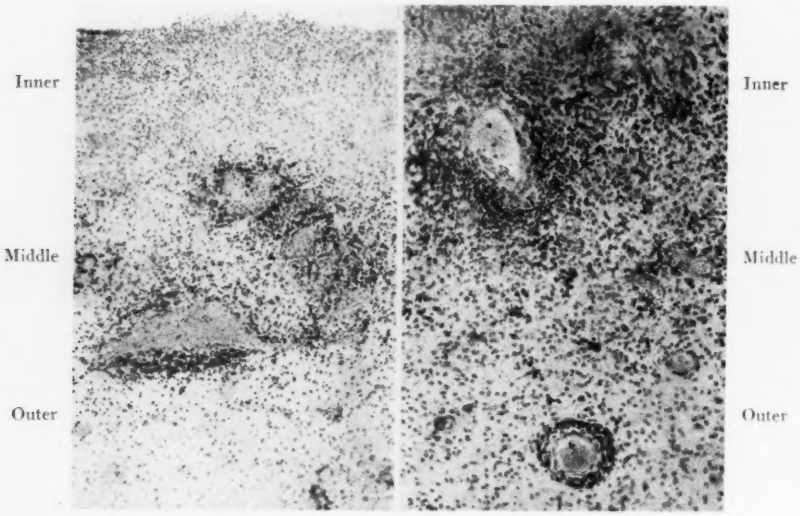

FIG. 11 A.—Case 8: Bright inner layer, dense middle and light outer layer of the abscess. (cresyl violet—×50.

FIG. 11 B.—Case 8: Various layers of the abscess and perivascular infiltrations in the middle and outer layers. (cresyl violet—×70)

Comment.—In this case, brain abscesses followed a simple upper respiratory infection associated with what appeared to be clinically a mild sinusitis. The mechanism of intracranial spread in similar cases has been studied by Kramer and Som.[36]

Case 9.—J. G., a man, age 42, entered the Montefiore Hospital, July 1, 1936. In December, 1935, he had suffered from a head cold, which lasted two weeks. Because of the frontal headaches the sinuses were drained. About a week later he suffered from a sharp pain radiating over the left side of the face; the next day that side of his face became paralyzed. Within the next few days, he noticed increasing weakness of his left hand and he began dropping objects. Progressively, the entire left upper and lower extremities became weak. He was operated upon, January 2, 1936, for a right midfrontal brain abscess. Four days later he developed diplopia on left lateral gaze, and his vision became severely impaired. During the following month, while he was at home, he appeared excessively emotional, laughed and cried without adequate provocation.

Neurologic Examination.—This revealed inattentiveness, confusion, memory lapses, and occasional delusions. There was a left spastic hemiparesis with hyperreflexia and

a Babinski sign on that side. Sensory examination disclosed a left hemihypesthesia for all modalities. There was left supranuclear facial palsy; the uvula deviated to the right and the tongue deviated slightly to the left. The pupils were irregular, the left slightly larger than the right, but both reacted to light and accommodation. The optic disks showed blurring. Following surgical exploration of the skull, the patient succumbed.

Laboratory Data.—The blood counts were normal; the Wassermann and Kahn tests were negative. Spinal puncture, performed July 19, 1936, revealed the following: Pressure 200 Mm. of water; cells, nine per cu. Mm., practically all lymphocytes. The total protein was 41.6 mg. per cent. Culture of spinal fluid was sterile. A spinal tap, repeated July 29, 1936, contained 290 lymphocytes per cu. Mm. Roentgenologic examination of the skull showed no bony abnormality.

FIG. 12.—Case 9: Abscess of the right hemisphere and lateral ventricle. (cresyl violet stain)

Autopsy.—The dura in the lowermost portion of the temporal fossa was slightly adherent to the underlying brain. The right hemisphere appeared larger than the left. There was a large area of softening extending from the right frontal to the parietal convolutions. The right lateral ventricle was completely constricted while the left was dilated. In sections through the beginning of the globus pallidus, the right lateral ventricle contained pus (Fig. 12). There was a serpiginous abscess within the right island of Reil (Fig. 12).

Microscopic Examination.—A complete coronal section through the striatum disclosed distortion of the right second and third frontal convolutions; the centrum ovale on that side was edematous. An extensive hemorrhage was present in the white matter of the right second frontal convolution (Fig. 12). In the right lateral ventricle, there was an abscess which consisted of a central necrotic area surrounded by a dense wall of polymorphonuclear leukocytes, lymphocytes, plasma and endothelial cells (Fig. 12). The vessels throughout the white matter of both hemispheres, more especially on the right side, showed perivascular infiltration. The ventricles were the seat of an extensive inflammatory process with numerous small multiple abscesses.

DISCUSSION.—*Factors Affecting the Spread of Infection:* Largely for anatomic reasons, purulent collections in the region of the supra-orbital ridge have an ominous significance. The frontal diploic vein emerges at the supra-

orbital notch and the anterior temporal vein close by. The diploic vessels communicate externally with the venous plexuses of the face and scalp, and internally with the meningeal veins and the adjacent sinus in the dura. The veins in the diploe of the frontal bone are continuous with the veins in the mucous membranes of the frontal sinus, affording ready passage of infection from the paranasal structures to the skull bones. The diploic vessels, especially during youth, are of such caliber as to be easily visualized by roentgenologic examination in 97 per cent of cases (Mosher[4]). Their importance lies in the fact that most of the circulation of the calvaria depends upon the veins and their innumerable small radicals in the diploe, rather than upon the arterial

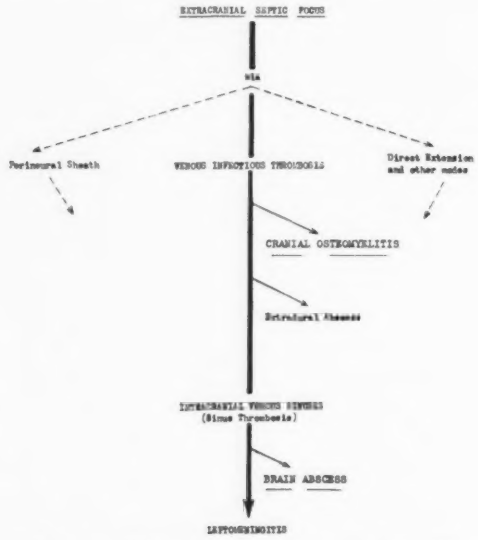

FIG. 13.—Diagram of the direct and indirect pathways leading from local infections about the head to intracranial complications.

supply. Any condition seriously affecting the venous circulation (thrombosis), therefore, jeopardizes the integrity of the bone. This fact is especially well illustrated in Cases 5 and 7 of our series.

The dura mater, which is virtually the inner periosteum of the skull, serves as an excellent barrier to the inward extension of infection. Usually, it is not until the inner table of the skull is involved by a carious process, that the danger of intracranial infection is imminent. In such circumstances the dura is always affected and becomes thickened and granular throughout the entire extent of the lesion in the bones.[16] Further protective adhesions are formed in the arachnoid. Other explanations of intracranial resistance on the basis of the hemato-encephalic barrier (King[25]), and of immunizing substances in the blood,[26] have recently been suggested.

When septic migration takes place from an extracranial source it may take any of several paths (Fig. 13), only one of which will be stressed in this study. Retrograde thrombosis into the emissary veins readily spreads in

the wide-open network of venous vessels and facilitates the rapid extension of the process in all directions. Bone necrosis ensues, generally, first in the outer table, as a result of which there is a discharge of pus under several areas of the scalp (Pott's puffy tumors). The clinical appearance of these fluctuant tumors is illustrated in Case 5. As the inner table is destroyed, similar collections of pus occur between bone and dura (extradural abscesses). The latter process also impairs arterial circulation to the calvarium, and further destruction of bone follows, until the typical worm-eaten appearance of the bone results. The ultimate extent of spread is limited by fibrosis of the marrow space. Mosher[4] points out that were it not for such zones of fibrosis about the sinuses, osteomyelitis of the skull would more often follow paranasal sinus infection.

The exact sequence between cranial invasion and intracerebral extension is still a matter of some controversy.[27, 29] It is not yet clear how the infection traverses the meninges and the dural sinuses without gross invasion or destruction of these intervening tissues. Some observers[2, 11, 33, 34] consider it probable that retrograde infection continues along the venous channels and extends directly into the soft cerebral substance, which is more vulnerable than the tough, highly vascular meninges. In all of our cases, however, some degree of meningeal involvement was found. Osteomyelitis is not invariably followed by cerebral abscess because intracranial invasion is often limited by a zone of reaction within the brain substance (Case 1). Such areas of localized encephalitis constitute, virtually, abortive abscesses, as pointed out by Putnam and Alexander,[34] Atkinson,[28] and others. When an abscess does develop, it is usually situated in the subcortex, especially in the white matter of the brain, where the veins originate and where cerebral circulation is poorest. The deep location is often a matter of serious surgical concern.

Other pathways of infection have been demonstrated. One is from the nasal cavities along the sheaths of the olfactory nerves.[29] Another, along the perivascular spaces of the brain, has been suggested by Atkinson,[28] Furstenburg,[17] and others, though a true perivascular "stalk" was not found by other observers, notably Carmichael, *et al.*[27] in a study of 75 cases. Suppuration may extend into the cranial cavity by contiguity or by direct implantation, particularly in the case of penetrating wounds.

The intermediate rôle of osteomyelitis may hold the explanation for the occurrence of a certain number of brain abscesses of obscure origin. Seventeen cases of doubtful or unknown etiology have been recently cited, and four more described by Yaskin, Grant, and Groff.[35] The recent studies of Kramer and Som[36] on the pathways of infection from the paranasal sinuses have revealed the presence of hidden or microscopic foci of osteomyelitis in the walls of the infected sinuses in ten cases which were complicated by intracranial infection. Minute foci of osteomyelitis in the petrous pyramid have been demonstrated by Fowler,[24] and others. Search for very small areas of suppuration in the skull, by special methods of exposure if necessary, as in

one of the cases here described (Case 1) may be helpful in revealing the origin of cryptogenic brain abscesses.

Pathologic Considerations.—The evolution of a brain abscess may be divided into three phases: (1) Phase of localized encephalitis; (2) phase of liquefaction, encapsulation; and (3) extension and rupture. Inflammatory changes begin about the thrombosed vessel in the centrum ovale and progress to necrosis of the tissues and suppuration. Spontaneous resolution and healing with scar formation has been suggested but never proven.[30] The usual progression is toward walling-off of the infection by a barrier of reactive elements, with the production of a fibrous capsule. Encapsulation begins within a week of infection and generally requires four to six weeks for completion. Surgical experience indicates that the walls of such abscesses are rarely firm enough to give a feeling of resistance to the exploring needle before the second or third week.[10] As the pathologic process progresses, the abscess increases in size until ultimately it ruptures into one of the ventricles (as in Cases 4 and 7) or into the subarachnoid space, with resultant pyocephalus or leptomeningitis. An unusual cause of death in the presence of cerebral abscess is that from complicating subarachnoid hemorrhage.

Several factors affect the growth and effective encapsulation of abscesses. Carmichael and his co-workers[27] suggest that an abscess must attain a size of 2 cm. or more in order to become encapsulated. As a rule, the older the abscess the better the degree of encapsulation. In the most virulent infections, death usually occurs before encapsulation can begin. Abscesses caused by less virulent organisms, particularly aerobes,[31] last a longer time, and attain considerable size, especially if they are located in one of the silent areas of the brain. Cahill[37] has observed that those of the temporal lobe have the thickest lining membranes, while acute cerebellar abscesses are rarely walled off. The largest abscesses in Evans'[1] series were those in the frontal lobe (average 3.5 to 4.5 cm.). The effect of medication, particularly sulfanilamide and sulfathiazole, on the acceleration or retardation of capsule formation, although frequently debated, has not yet been demonstrated pathologically or experimentally.

The nine cases of brain abscess presented in this series originated from relatively common infections about the head. One (Case 1) originated from a parapharyngeal abscess, another from a peritonsillar abscess (Case 2). Furunculosis of the face and scalp was primarily responsible for the brain abscesses found in Cases 4 and 7, and secondarily so in Case 3. Four cases were of rhinogenic origin (Cases 5, 6, 9 and 10), complicating in several instances what appeared to be a clinically mild upper respiratory infection. In one of our patients, diffuse osteomyelitis of the skull and brain abscess followed a fulminating sinus infection which developed after the aspiration of water into the nose while swimming (Case 5). Gross or microscopic foci of cranial osteomyelitis were found in those cases where special search for such lesions was made (Cases 1, 3, 5, 6 and 7), while the pathologic process (empyema of a paranasal sinus) strongly suggested the presence of bony involve-

ment in the other cases. Microscopic foci of bone destruction have been demonstrated by others in connection with sinus suppuration.[4, 17, 36] It appears from our material that cranial osteomyelitis is frequently the intermediate step between a local infection about the head and a complicating abscess of the brain.

Clinical Correlations.—Knowledge of the various stages in the pathogenesis of brain abscess may be of great aid in the interpretation of clinical symptoms. As the pathologic processes of the cranial and intracranial extension unfold, certain heralding symptoms appear, and it is from these that the earliest diagnosis of complications might be made. Repeated chills in the presence of an infection about the head, particularly one in the region of the frontal emissary veins, point to possible extension of thrombophlebitis into the skull with the initiation of osteomyelitis. Bone caries are not produced until seven or ten days after invasion, hence, frank roentgenographic changes are not evident within the first two weeks of the illness. The occurrence of pitting edema of the forehead or of localized swellings in the scalp (Pott's puffy tumors) are early and cardinal signs of osteomyelitis in the flat bones of the skull. The spinal fluid during this phase, except for occasional increase in pressure, shows no abnormality.

The phase of osteomyelitis is characterized by a toxic, febrile course, leukocytosis and frequently chills. There is often a latent period of apparent clinical improvement. Then, after days or weeks, septic temperature, headache, and vomiting occur; then nuchal rigidity, focal neurologic signs, increased spinal fluid pressure and pleocytosis indicate the presence of brain abscess. The spinal fluid findings associated with the presence of encapsulated brain abscess in the second to fourth week of the illnesses represented in this series were: Slight increase in the spinal fluid pressure (85 to 230 Mm. of water); cell counts of eight to 200 cells per cu. Mm., with an average of less than 50 per cent polymorphonuclear leukocytes; one plus to two plus albumin; and protein values of 41 to 102 mg. per cent.

According to McKenzie,[21] Fincher,[38] Adson and Hempstead,[39] King,[40] and Bucy and Haverfield,[7] and others, osteomyelitis of the skull inadequately treated commonly results in fatal brain abscesses. Early diagnosis of osteomyelitis, before the evidence of roentgenographic changes, and complete removal of all infected bone with interruption of the venous channels in the bone which carry the infection inward is the only rational treatment. Discerning surgical management, based upon fuller understanding of the pathogenesis of brain abscess has drastically reduced the mortality from this complication.

CONCLUSIONS

Brain abscess may follow simple infections, other than otitic, about the head. Clinical and autopsy studies of nine cases of brain abscess of uncommon origin are presented. Two cases originated from infections in the pharynx;

three were secondary to furunculosis of the face and scalp; and four were complications of paranasal sinus infection.

Osteomyelitis of the skull is frequently the intermediate stage between primary infection and brain abscess. Several illustrative cases are presented.

The pathology of spread is described and correlated with pertinent diagnostic and therapeutic considerations.

Painstaking search for small areas of suppuration in the cranial bones may reveal the explanation for many cases of "cryptogenic" intracranial infections.

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GASTRIC POLYPOSIS

REPORT OF A CASE OF "*polyadenomes en nappe*," DIAGNOSED GASTROSCOPICALLY

WILLIAM G. HEEKS, M.D.,

AND

WILLIAM T. GIBB, M.D.

NEW YORK, N. Y.

FROM THE GASTRO-INTESTINAL CLINIC AND SURGICAL SERVICE "A" OF ST. LUKE'S HOSPITAL, NEW YORK, N. Y.

GASTRIC POLYPOSIS, by which term single adenomatous polypi are properly excluded, is an uncommon condition. Only about 100 authenticated cases have been reported in recent comprehensive reviews of the literature. Balfour[1] states that in 69,000 celiotomies performed at the Mayo Clinic, of which 8,000 were primarily gastric operations, only one case of gastric polyposis was encountered. Brunn and Pearl,[2] in a survey of the literature from 1820 to 1925, report 84 cases, five of which they observed personally. The first 49 cases were found only at autopsy. They state that Tigler found 14 benign gastric tumors in 3,000 autopsies. They also quote figures from Doering and from Verse. Doering, in 50 cases involving the entire gastro-intestinal tract, noted that the stomach was involved in only five, while Verse reported 55 cases with the stomach involved in only five, but in none of these was the stomach alone affected.

Cruveilhier,[3] in 1833, was the first to give the distinction of a disease entity to gastric polyposis. The first case diagnosed at operation was that of Wegele,[4] in 1909. Chosrojeff[5] made one of the earliest clinical diagnoses, in 1912, when gastric lavage revealed blood and particles of polypi. The first roentgenologic diagnosis, according to Balfour,[1] was made by Carmen in 1919. A gastroscopic diagnosis of multiple single polypi was first made by Schindler,[6] in 1922. We believe this to be the first proven diagnosis of *"polyadenomes en nappe"* made with the flexible gastroscope.

Etiology.—Many opinions have been expressed concerning the causative factor of gastric polyposis and certainly the exact etiology is still unsettled. Some observers favor a congenital origin and believe the polypi to arise from fetal anlagen. It is true that in multiple polyposis involving the large bowel there is a definite hereditary factor, but this has not been demonstrated in gastric polyposis. Most authors favor chronic irritation as the inciting cause, and Menetrier[7] suggests the influence of alcohol. Meyer[8] reports a case in which syphilitic gastritis may have been the underlying cause.

Pathology.—The classic work on the pathology of adenomatous gastric polypi was published in 1888 by Menetrier,[7] who described two varieties: (1) *"Polyadenomes polypeux"*; and (2) *"polyadenomes en nappe."*

"Polyadenomes polypeux" are classified as the discrete polypi with independent attachments, either pedunculated or sessile. They are soft, gray, ashy,

brown or red in color, and while their size is variable, it rarely exceeds 2 cm. In number they range from one to more than 300, and, although most common in the region of the pylorus, they may be found in any part of the stomach. Microscopically, they are composed largely of glandular tissue, and the glands are lengthened, often tortuous, occasionally compound, and devoid of pepsin

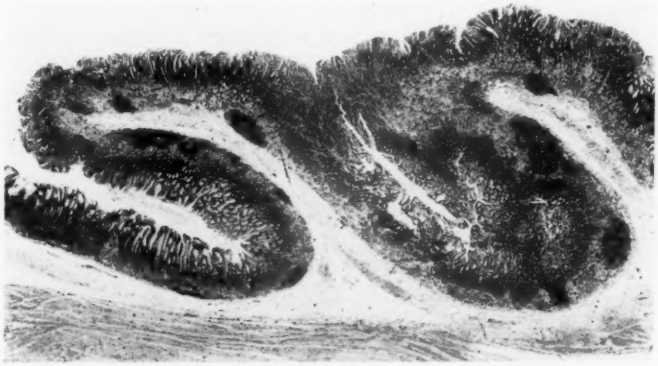

FIG. 1.—Photomicrograph illustrating the general pattern as described by Menetrier.

FIG. 2. FIG. 3.

FIGS. 2. and 3.—Roentgenograms showing polypoid type of the gastric lesion.

cells. Cyst formation is common when the excretory ducts are obstructed by connective tissue.

In describing Menetrier's second group, *"polyadenomes en nappe,"* we can best quote his original paper: "In contrast to some of the smaller pedunculated and sessile tumors arising from simple glandular hyperplasia there is another lesion, essentially a mucosal hypertrophy, in which the glands assume considerable proportions but with the more diffuse and general alteration in-

volving large areas of tissue, forming large hypertrophied plaques rising plume-like above the rest of the mucosa, or even involving nearly the entire stomach, the internal aspect of which then appears tufted and wavy with large folds giving a marked resemblance to cerebral convolutions." He attributes this descriptive phrase to Briquet.

Menetrier continues: "These are glandular hypertrophies with overgrowth of the epithelial covering, with corresponding increase in the basement membrane and of the interglandular connective tissue. The epithelium is modified into various forms but it is always laid down in regular manner; the glandular

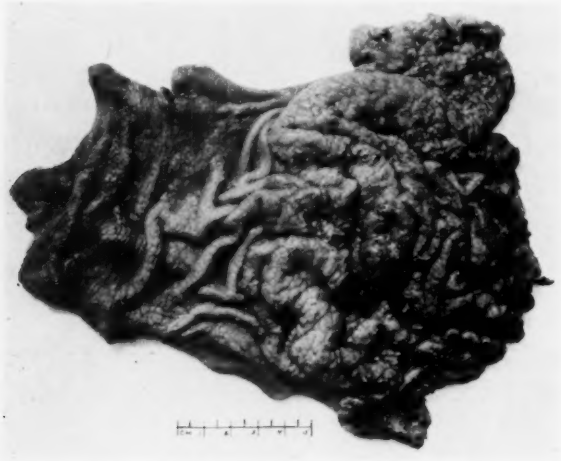

FIG. 4.—Photograph of the gross specimen.

tubes often maintain their upright position, may reduplicate themselves and describe sinuosities, there may be found areas with cystic cavities, but essentially, and it is a cardinal principle, the glandular form persists, the membrana propria is preserved, none of the epithelial cells pass beyond it, and finally, and above all, something which must be considered glandular hyperplasia, never do the proliferated cul-de-sacs pass the basement membrane which is their normal habitat, the muscularis mucosa always forms a limiting membrane for them, easily identified and never broken at a single point.

"It is the glandular hypertrophy, and it alone, which determines the thickness of the mucosa. The glands increase in height keeping almost entirely in a straight line, and reach unusual proportions, being five or six times their normal length, while their diameter increases much less and sometimes even diminishes. This long glandular tube is permeable, its orifice is preserved and it is lined with low cuboidal epithelium. The stroma of the mucosa is generally a little thickened and is stretched out like the glands. Rising from the depths are more thickened fibrous bands, each forming an axis around which the tallest glands are grouped in protruding tufts, distinct one from the other and separated by ridges, at the bottom of which are seen the shallowest glands and where the mucus they secrete accumulates.

"Such is the general pattern. This regular hypertrophy follows the whole extent of the mucosa, thereby becoming too large for the cavity it lines and must, to accommodate itself, fold itself into waves and protruding convolutions which carry in their center prolongations of the cellular tissue. It is, therefore, a pathologic and permanent exaggeration of the normal gastric mucosa.

"It is a simple hypertrophy, a benign noninfectious lesion. Although the lesion is benign, it does have affinities with more malignant states and these lesions may be transformed into epitheliomas and cancers."

Kirklin and Broders[9] aptly state that although polypi generally are benign lesions, they maintain their benign state somewhat precariously. Christopher[10] reports an interesting case of this second group which had undergone malignant changes.

Symptoms and Signs.—All writers on the subject are generally agreed that the symptoms and signs are obscure. Frequently, the only complaint is of mild abdominal discomfort, usually developing after meals and in some cases relieved by the ingestion of food or soda. Hematemesis and melena may be noted. Two characteristic findings, according to Meyer,[8] are achlorhydria and an increase in gastric mucus which appears much like finely divided, slightly coddled white of egg. It has been claimed that these changes are produced by the associated inflammatory reaction rather than by the polypi themselves. Frequently, a secondary anemia is present and may be confused with pernicious anemia because of the associated achlorhydria. In the collected series of Brunn and Pearl, previously noted, abdominal distress was present in 28 per cent; vomiting, anorexia, constipation, diarrhea and weakness each in about 17 per cent; and hematemesis in 8 per cent.

FIG. 5.—Photomicrograph showing the characteristic appearance of a papillary process.

Diagnosis.—The presence of achlorhydria, myxorrhea and gastric hemorrhage demand a consideration of the lesion. Essentially, however, the diagnosis must be more conclusively made by the use of the two morphologic aids at our disposal, roentgenography and gastroscopy. In recent years, increased

roentgenologic diagnosis is evident by the relative frequency with which articles by roentgenologists have appeared in the literature.[9, 11, 12, 13, 14, 15] This is undoubtedly accounted for by improved roentgenologic technic and more detailed fluoroscopy. Nevertheless, in large clinics it is impossible to study minutely every case referred for routine roentgenologic examination of the gastro-intestinal tract, and some lesions will escape diagnosis. It is beyond the scope of this paper to describe the roentgenologic signs of gastric polyposis, but we would emphasize the fact that the differentiation of tumors from hypertrophied folds of mucous membrane may present a difficult problem. In cases of chronic hypertrophic gastritis, large rugal folds in cross-section may exactly simulate small polypi. In one of our cases of diffuse gastric polyposis, or *"polyadenomes polypeux"* roentgenologic diagnosis was not made correctly until after the tumors had been seen through the gastroscope.

There can be no doubt that routine examination by gastroscopy of all patients presenting gastric symptoms will make possible earlier diagnoses not only of benign but also of malignant lesions. This procedure, in experienced hands, is safe and can be carried out with minimal discomfort to the patient.

Differential Diagnosis.—Several conditions must be considered in differential diagnosis, among which may be mentioned carcinoma, particularly the polypoid type, lymphosarcoma, hypertrophic gastritis, gastric syphilis, bezoars, and any other lesions which may cause achylia gastrica.

Prognosis.—As Menetrier stated, while gastric polyposis is essentially a benign lesion, it does have affinities with more malignant states. Brunn and Pearl,[2] in their first paper reporting 84 cases, found an incidence of malignancy of 12 per cent. In a later paper, these authors[16] concluded that more than 12 per cent were malignant.

Treatment.—There is general agreement that surgery offers most in the way of treatment, and partial gastric resection should be performed wherever possible. This is particularly true when the incidence of malignancy is considered as something over 12 per cent, in contrast to an operative mortality which should not exceed 7 per cent in qualified hands. Brunn and Pearl[16] state that symptoms have been present in certain cases for from 15 to 30 years without any evidence of malignant degeneration. However, a sudden increase in severity of symptoms should warn one of the possible onset of this complication.

Case Report. Hosp. No. A-03996: The patient, white, female, age 35, single, was first admitted to St. Luke's Hospital, November 11, 1938, with a chief complaint of epigastric pain one hour after meals coming in recurrent episodes during the past nine years. Nine, six, and five years ago she suffered attacks of pain which did not radiate but were associated with nausea and vomiting. Alkalies gave no relief. There was no hematemesis nor melena. Numerous gastro-intestinal series at various hospitals all showed the presence of a duodenal ulcer. On dietary regimens, which she did not conscientiously follow, temporary relief was obtained. She had always been subject to nervous attacks, and for the past two months had been nervous all the time, had little appetite, and had lost five pounds, present weight 98 pounds. Three weeks ago she had her last attack of burning epigastric pain occurring an hour after meals and associated

with nausea and vomiting for two days. She was placed on a bland diet and given bismuth and soda powders, with prompt relief.

The only other significant facts in the history were that she smoked 20 cigarettes daily, and used alcohol "occasionally." Physical examination contributed little other than that she was a thin, fairly well-developed and well-nourished individual, with slight epigastric tenderness but no palpable mass.

Laboratory Data.—Hemoglobin 80 per cent, R.B.C. four million; uranalysis negative; and serology negative. A gastric analysis apparently was omitted.

Gastro-intestinal series, made in the clinic on October 17, 1929 and September 23, 1937, revealed the presence of a duodenal ulcer. A series made October 28, 1938 was reported as follows: "Stomach is large in size and normal in position. In the pars media a polypoid type of growth is seen extending into the lumen of the stomach; beyond the pylorus a regular cap filled. At the sixth hour the stomach had completely emptied. The appearance presented is that of new growth."

Gastroscopic examination was performed November 12, 1938, and our report follows: "The 55° gastroscope was readily passed, and a normal angulus and antrum seen. The pylorus was not visualized. The rugae of the entire posterior wall extending distally to the angulus were finger-like in size, velvety, finely nodular and congested in appearance, actually resembling cerebral convolutions." Never having seen a similar pattern, we were unable to state whether it represented a benign polypoid type of hypertrophic gastritis or a true carcinoma, but we felt that it should be classified as a precancerous lesion.

Operative Pathology.—"The stomach was hypertrophied. An indurated, whitish spot on the anterior surface of the duodenum proved to be a chronic ulcer. When the stomach was opened, the mucous membrane of the posterior wall was seen to be hypertrophied and lay in succulent folds. No evidence of carcinoma nor of metastases was seen." After partial gastric resection, a retrocolic Pólya-type of gastrojejunostomy was performed.

Pathologic Report.—Macroscopic Examination: Doctor Knox. "Specimen consists of a stomach measuring 13.5 on the lesser and 18 cm. on the greater curvature. A small portion of duodenum adjacent to the pylorus is included. The serosal surface is clear and pale pink. In the upper portion is an incision into the mucosa measuring 5.5 cm. which has been sutured. A small amount of mesentery is attached. No lymph nodes are found. The mucosal surface of the proximal portion shows hypertrophy of the rugae, giving an appearance similar to the exterior of the cerebrum. The mucosa is intact except at the site of the incision. On section, the mucosa is hypertrophied and there is some thickening of the muscularis.

"Microscopic: Sections show a portion of the normal mucous membrane of the stomach and also the tall, branching and overhanging rugae, which simulate a papillary adenomatous growth. This area shows an increase in all the cells of the mucous membrane, the epithelium forming long, usually straight, very narrow lumina in most areas. Occasionally the local reduplication is so great as to result in tortuous cysts in the deeper portion of the mucosa. This high degree of differentiation of the cell types of the mucosa distinguishes the lesion from a polyp. The cells are hypertrophied as well as greatly increased in number, but they are regular in outline and normal in staining reactions, and the type of overgrowth does not suggest a true neoplasm. *Pathologic Diagnosis:* Papillary, adenomatous hypertrophy of mucosa of pyloric portion of stomach."

The patient has made excellent progress, and when last seen, in December, 1939, one year after operation, she stated that she felt fine; had no gastric symptoms; and had gained 14 pounds in weight.

SUMMARY AND CONCLUSIONS

(1) A discussion of gastric polyposis, and a detailed description of Menetrier's histologic classification are given.

(2) The symptoms and signs of the disease are obscure, but vague

gastric discomfort, myxorrhea, achlorhydria and hematemesis may suggest the diagnosis.

(3) Roentgenologic and gastroscopic examinations are the chief aids in diagnosis.

(4) A case is reported which we believe to be the first diagnosed by gastroscopy, and proved by operation and pathologic examination, to be one of *"polyadenomes en nappe."*

(5) Although the incidence of malignancy is thought to be relatively low, the treatment of the disease should be surgical.

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ADENOMA OF THE PANCREAS

CASE REPORTS

S. S. QUARRIER, M.D.,
AND
C. T. BINGHAM, M.D.
HARTFORD, CONN.

REPORTED CASES of tumors of the islet cells of the pancreas are rather rare. Frantz[1] was able to collect only 96 cases up to December, 1939. The first case of such a tumor which was recognized and successfully operated upon in the Hartford Hospital was quite characteristic in every detail. We have, therefore, thought it worthy of presentation. A brief summary of three other cases from the records of the Hartford Hospital has been added because of unusual pathologic findings.

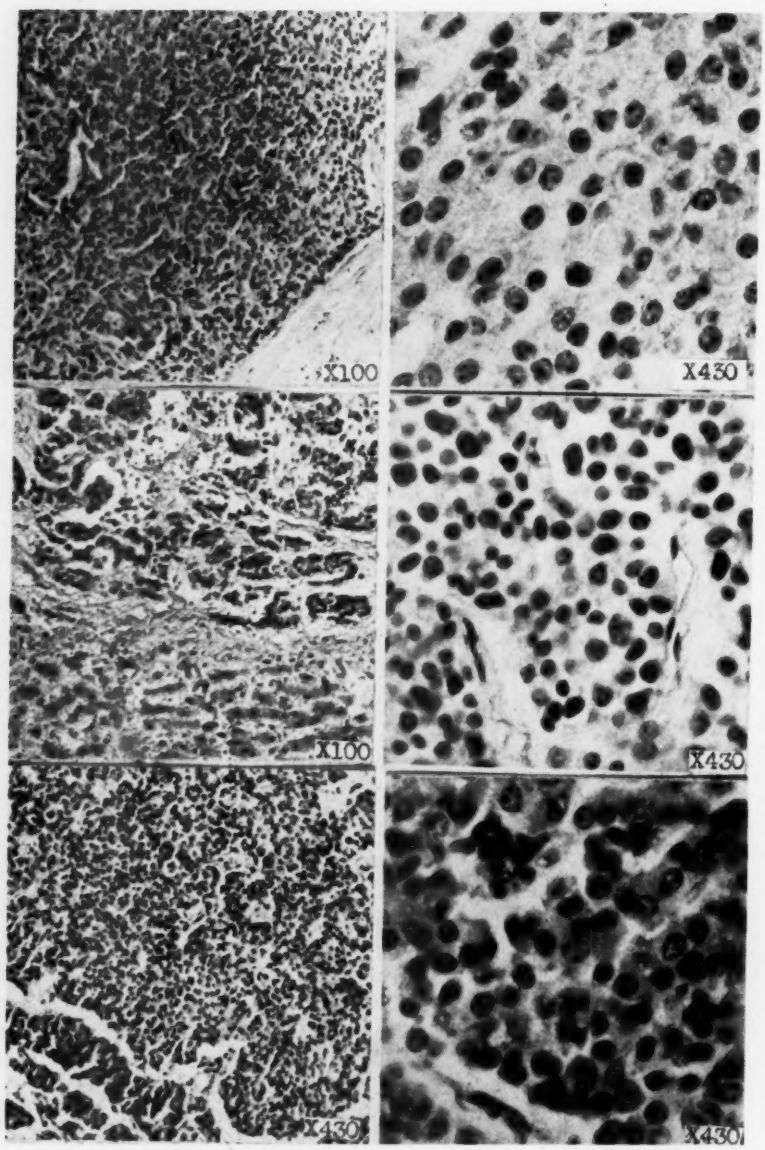
Case 1.—Hartford Hospital No. 395416: B. T. R., age 48, American housewife, was admitted, August 15, 1940, with the chief complaint of recurrent attacks of unconsciousness. These attacks occurred usually in the morning and before breakfast, and lasted from one to four hours. They varied in severity from a slight degree of drowsiness and disorientation to semicoma and even to complete unconsciousness. At times the patient was seen to have difficulty in swallowing or talking. Her speech became guttural or unintelligible. At other times she appeared white, cold, and rigid. Occasionally, she seemed flaccid yet unable to move, and sweated profusely. Her physician found her blood pressure as high as 220/110 during one of these attacks. The patient had been having these attacks with increasing frequency for five months before admission. She was otherwise a well-adjusted, normal person who had had no serious illnesses in the past. On physical examination nothing abnormal was found except a patch of old chorioretinitis in the right eye; blood pressure 148/100; slight enlargement of the heart; and an increase in the deep reflexes.

Complete laboratory examinations of the blood, including blood count, sedimentation rate, and Hinton test, were negative. The analyses of spinal fluid and urine, including urine diastase, were entirely normal. Roentgenograms of the skull, electrocardiogram and electro-encephalogram showed no deviation from normal. The only abnormal laboratory finding was a fasting blood sugar of 30 mg. per cent on one occasion and 32 mg. per cent on another. The glucose tolerance test showed a fasting level of 56 mg. per cent, and the following levels on hourly samples: 148, 182, 182, 136, 56, and 46 mg. per cent.

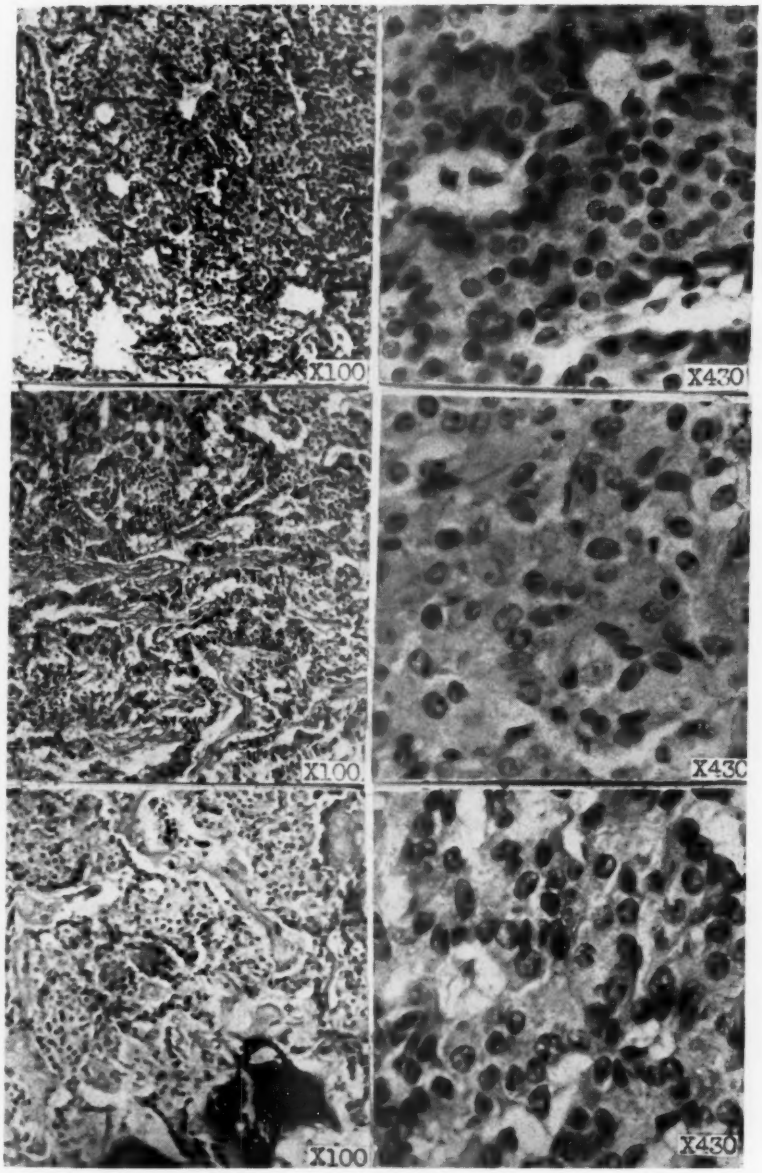
It was found that the patient's attacks could be prevented by the taking of nourishment and that the attacks themselves could be aborted by the intravenous administration of glucose.

Hyperinsulinism due to an adenoma of the islet cells of the pancreas seemed the most likely diagnosis in this case, particularly as it fulfilled the triad of requirements as outlined by Whipple,[2] namely:

(1) Attacks consisting of:
  (a) Vasomotor collapse.
  (b) Restlessness, spasm, and convulsions.
  (c) Confusion, disorientation, and coma.
(2) Blood sugar levels of 50 mg. per cent, or less, during such attacks.
(3) Relief of symptoms by administration of glucose or taking of nourishment.



Top: FIG. 1—Case 1: Encapsulated islet cell adenoma.
Middle: FIG. 2—Case 2: Metastasis to liver of islet cell carcinoma.
Bottom: FIG. 3—Case 3: Nonencapsulated islet cell adenoma.



Top: FIG. 4.—Case 4: Islet tumor cells around vascular spaces.
Middle: FIG. 5.—Case 4: Islet adenoma with marked fibrosis.
Bottom: FIG. 6.—Case 4: Islet adenoma with calcification.

It is generally conceded that surgical removal is the treatment of choice, as prolonged medical treatment has three disadvantages: (1) Mental deterioration from recurrent hypoglycemic reactions; (2) personal injury from falls during the attacks; and (3) malignant degeneration. Medical treatment was, therefore, not tried, and the patient was operated upon September 21, 1940.

Operation.—Preoperatively, an infusion of 1,500 cc. of a solution of 5 per cent glucose and saline was administered. Ether anesthesia was employed, as this mobilizes liver glycogen more effectively than other anesthetic agents. A transverse incision above the umbilicus, through both recti muscles, as described by Whipple was used, and exposure of the pancreas was accomplished by opening the gastrocolic omentum. On the anterior surface of the pancreas, near the inferior edge, and at the junction of the tail and the body was a 1.5 cm., vascular, purplish-red, firm tumor, which was immediately recognized as an adenoma of the pancreas. Careful visualization and palpation of the pancreas revealed no further pathology. By sharp and blunt dissection the tumor was excised, bleeding was controlled with fine silk ligatures, and the abdomen was closed in layers without drainage, using interrupted silk sutures.

Postoperative Course.—The patient made an uneventful convalescence, and was discharged two weeks after operation. The postoperative fasting blood sugars ranged between 72 and 95 mg. per cent. Chart 1 shows, graphically, the pre- and postoperative fasting blood sugar readings. Follow-up of nine months on this patient revealed complete relief from her attacks.

Pathologic Examination.—Gross: The specimen was a lobulated tumor, 1.5 cm. in greatest diameter, partially surrounded with a delicate fibrous capsule. *Microscopically,* sections (Fig. 1) showed a cellular tumor with moderate sized oval granular nuclei and prominent nucleoli. The cells were similar in type to the islet cells in the adjacent pancreas. Mitoses were rare. There was a vascular stroma of fibrous tissue separating the lobules, and in most places a well-defined fibrous capsule. There was no evidence of invasion into the pancreas, but in one area there were tumor emboli in vascular spaces.

A review was made of the Hartford Hospital records, and three other cases of tumors of the islands of Langerhans were found.

Case 2.—Hartford Hospital No. 215803: W. H., age 73, white male, was admitted to the medical service, in 1928, because of morning fainting attacks for three weeks previous to admission.

Course.—Patient was unconscious on admission and only lived three days. One hour before death his blood sugar was 21.4 mg. per cent.

Autopsy.—No. 452: Revealed a 3 cm. carcinoma of the islands of Langerhans in the tail of the pancreas, with metastases to the liver and regional lymph nodes.

Pathologic Examination.—Microscopic: Section showed a tumor composed of masses of cells surrounded by a dense avascular stroma. The cells had small, oval, granular nuclei, and were similar to the islet cells in the adjacent pancreas. Mitoses were rare. There was little anaplasia, but definite tumor cell infiltration of surrounding fibrous tissue and pancreas. Some of the larger blood vessels contained groups of tumor cells. In places there was degeneration of amorphous hyaline fibrous tissue, with calcification. The metastases in the liver (Fig. 2) and lymph nodes were similar in cytology to the original tumor.

Case 3.—Hartford Hospital No. 276892: A. P., age 59, white male, was admitted to the medical service, in 1933, because of morning dizzy spells, collapse, sweating, disorientation, and convulsive spasms for seven years. These attacks were relieved by the intake of sugar. Fasting blood sugar specimens varied from 26 to 55 mg. per cent.

Operation.—July 11, 1933: Dr. A. M. Rowley. A very careful search of the whole pancreas was made but no tumor was found. In exploring the pancreas considerable bleeding was encountered which was difficult to control.

Postoperative Course.—The patient died a few hours after the operation from shock and hemorrhage.

Autopsy.—No. 1230: This revealed a 1.2 cm., partially encapsulated tumor deep in the substance of the pancreas, and 7 cm. from the tip of the tail.

Pathologic Examination.—Microscopic: Sections of this tumor showed masses of tumor cells, arranged around endothelial-lined vascular spaces, with very little fibrous tissue stroma (Fig. 3). The cells resembled islet cells of the adjacent pancreas. No mitoses were seen. The capsule was completely lacking in places, in fact, there was tumor cell penetration as a mass into the pancreas, but no actual infiltration through the normal tissue. No blood vessel invasion was seen.

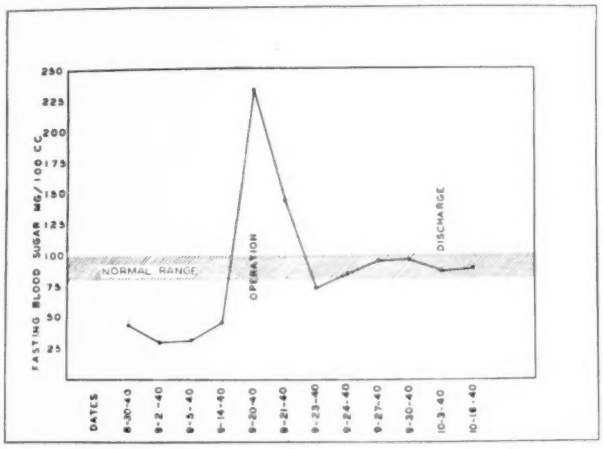


CHART 1.—Pre- and postoperative fasting blood sugar readings.

Case 4.—Hartford Hospital No. 242564: E. E., age 20, white female, was admitted to the Medical Service, in 1930, because of attacks of morning unconsciousness, tremor, and mild convulsions for one and one-half years. The attacks were prevented by ingestion of sugar. Fasting blood sugar specimens varied from 23 to 57 mg. per cent.

Operation.—December 3, 1930: Dr. A. M. Rowley. Three tumors from the pancreas and one from the left adrenal were excised.

Postoperative Course.—The patient died on the second postoperative day, with hyperpyrexia.

Autopsy.—No. 720: This revealed no significant pathology except the evidence of a recent abdominal operation.

Pathologic Examination.—Gross: The surgical specimens showed three discrete tumors of the pancreas, varying in size from 2 to 4 cm. The tumor from the left adrenal measured 3 cm. in diameter, and was not encapsulated.

Microscopically, the three pancreatic tumors showed one well-encapsulated and two partially encapsulated adenomata of the islands of Langerhans. There was considerable variation in the cell arrangements in the three tumors, but the cell type was quite similar to, and resembled, islet cells of the pancreas. In one, the cells were arranged in ribbon-like cords which surrounded endothelial-lined vascular spaces (Fig. 4). In the second, fibrous tissue proliferation separating the tumor cells into small clumps was a more marked feature (Fig. 5). In the third, the supporting fibrous tissue showed hyaline change and areas of amorphous calcium deposit (Fig. 6). No mitoses were seen. In one of the adenomata, tumor cells were found in some of the vascular spaces. An acid-alcohol extract of this tumor tissue was injected into rabbits, which initiated an hypoglycemic shock, that was immediately relieved by intravenous administration of glucose.

Pathologic Examination.—Microscopic: Sections of the tumor of the left adrenal showed a primary adrenal carcinoma, the cytology of which differed entirely from the pancreatic adenomata. Extract of this adrenal tumor when injected into rabbits failed to cause hypoglycemic shock.

SUMMARY

A typical case of islet cell adenoma of the pancreas, with relief following excision is reported; and three other interesting cases are mentioned.

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THE MANAGEMENT OF URETERAL CALCULI

CHARLES C. HIGGINS, M.D.

CLEVELAND, OHIO

THE MAJORITY of ureteral calculi are formed primarily in the kidney. At this site they may be retained, or may pass down the ureter, where they may become lodged or pass spontaneously into the bladder. Rarely may a calculus develop *ab initio* in the ureter in the presence of diverticula or sacculations, the latter being associated with a stricture in the ureter itself.

That a stone should not develop primarily in the normal ureter appears logical, inasmuch as the crystalloids essential for calculous formation are washed into the bladder by the urinary stream. The origin of a calculus in the ureter, however, may be a calcareous plaque developing on the mucosa, as mentioned by Caulk, in which instance the plaque acts as a nucleus for stone formation. From the standpoint of preoperative and postoperative investigation and care, however, we may consider the kidney itself as the site of calculous formation. To minimize the significance of intensive preoperative study of the etiologic factors involved, and their correction and eradication during the operative procedure or during the postoperative regimen, is to invite recurrent formation of stones.

The most acceptable hypotheses of the causation of calculi in the urinary tract are: (1) Focal infection; (2) stasis; (3) infection of the urinary tract, especially with urea-splitting organisms; (4) vitamin A deficiency; (5) metabolic diseases, in which an increased excretion of crystalloids occurs in the urine; (6) hyperparathyroidism; and (7) local disease of the renal papillae.

From clinical and experimental observations, it is apparent that no single etiologic factor is responsible for the formation of all calculi. With our present conception of calculous disease, it is essential to ascertain the presence or absence of the factor or factors responsible for stone formation in each case. A presumption of their absence is fraught with the possibility of a high morbidity. Roentgenologic investigations reveal that the majority of ureteral calculi become lodged in the pelvic portion of the ureter. This hesitation in the descent of the calculus may be temporary, in which case it passes into the bladder or becomes impacted, thus preventing further movement. The arresting of the downward progress of a calculus in the ureter may be satisfactorily explained by the anatomic characteristics of the normal ureter. It has been demonstrated in cadavers that the caliber of the ureter varies in its different portions.

Constriction may occur in five locations in the normal ureter (Fig. 1); namely, (1) at or just below the junction of the ureter and the renal pelvis; (2) at the point where the ureter crosses the iliac vessels; (3) at the base of the broad ligaments in the female, and the vas deferens in the male; (4) at the point where the ureter enters the external muscular layer of the bladder, the so-called juxtavesical constriction; and (5) at the ureteral orifices. Between

these constrictions the ureter is widened into spindles, the diameter of which decreases progressively downward.

In addition to the points of constriction mentioned, physiologic angulations of the ureter may occur at two points: First, at the site where the ureter crosses the iliac vessels and dips downward into the true pelvis; and second, at the *pars juxtavesicalis* which presents a physiologic angulation of from 90° to 135°. Undoubtedly, these conditions in the normal ureter explain, in a large proportion of cases, the incidence of ureteral calculi at various levels in the ureter.

In this series of 350 cases, 77.4 per cent of the stones were observed in the lower ureter, of which 63.3 per cent were in the pelvic portion, and 14.1 per cent in the intramural portion. The positions of the calculi in this total series are shown in Table I.

TABLE I

POSITIONS OF CALCULI IN 350 CASES

Right upper ureter	14 cases
Left upper ureter	16 cases
Right midureter	21 cases
Left midureter	22 cases
Right lower ureter	128 cases
Left lower ureter	143 cases
Bilateral ureteral calculi were present in six cases:	
Right lower ureter and left lower ureter	3 cases
Right lower ureter and left upper ureter	1 case
Right midureter and left midureter	1 case
Right midureter and left lower ureter	1 case

MANAGEMENT

The procedures to be utilized in the management of ureteral calculi are: (1) Expectant and medical; (2) manipulative procedures; and (3) surgical intervention. Several factors influence the type of treatment to be advocated in the individual case.

Expectant Treatment.—In eliciting the history from patients with calculous disease, we are warranted in assuming that a large percentage of ureteral calculi are expelled spontaneously. Many patients cite repeated episodes of pain followed by the passage of a calculus. In the present series of 350 cases, 18.9 per cent of the calculi passed spontaneously during expectant treatment. During this period fluids should be forced and urinary antiseptics prescribed, if necessary. The prescribing of drugs as an aid in the expulsion of calculi in the ureter is recommended by some authors. Hager[1] recommended the subcutaneous injection of 1 cc. of 1:2000 solution of prostigmin at three- or four-hour intervals for four doses to stimulate passage of ureteral calculi.

O'Conor[2] reported the results of treatment with this drug in 52 patients. The cases were selected carefully before its administration. In 30 cases in which expulsion occurred, the procedure appeared to hasten the passage of the stone in 23 instances. Of six cases in which calculi of larger size did not continue to descend over longer periods of time, in five the stone passed into the bladder, and in one it was arrested in the ureteral orifice following the

administration of this drug. In 16 patients, meatotomy, dilatation and multiple catheters or bougies were employed without effecting passage of the stone. In the presence of a large lower ureter, and in the absence of complications necessitating surgical intervention, prostigmin was employed, followed by rapid descent or expulsion of the calculus in 12 of the 16 patients. He concluded, therefore, that of the 66 patients treated, prostigmin was employed as an additional aid in 52, and in 18 of these the clinical response was so striking that the efficacy of the drug in selected cases is beyond doubt.

Scholl,[3] in treating 15 personal cases in a similar manner, observed, in seven instances, that the drug exerted a beneficial action.

Of 19 cases in which I have employed the drug, in eight instances, within four days after the medication was prescribed, the stone was expelled from the ureter. In four additional cases the stone passed within one week, while in seven instances the progress of the calculus was not affected.

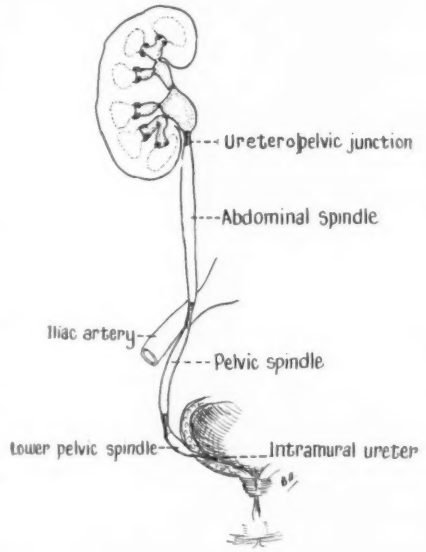

FIG. 1.—Diagram illustrating the sites of constriction in the normal ureter.

It is known that in patients who have passed stones previously, progressively larger stones may be expelled than would occur when the initial stone passes into the ureter. Similarly, a small calculus that has just occupied the ureter is more apt to pass spontaneously than if it has been lodged in the ureter for a longer period of time.

In patients in whom expectant treatment is advocated, careful observation is essential. Progress roentgenograms to follow the course of the calculus are required. When the patient's symptoms subside, either a complete block has occurred, or urine is passing around the stone into the bladder. If intravenous urographic study reveals a complete block, in which instance the pelvis and calices are not visualized, unless prompt additional treatment is employed, complete destruction of the kidney may result. To delay instrumentation for too long a period of time in selected cases of ureteral calculi, or failure to recommend surgical intervention if deemed advisable, may be attended by little success. Such postponement may be followed by loss of the kidney, or even death of the patient.

Several factors determine whether manipulative procedures are advisable or surgical intervention is required. These are:

(1) *Economic Status of the Patient.*—Just as the economic status of a patient may influence the treatment to be instituted in medical problems ex-

traneous to the urinary tract, so may it influence the treatment to be advocated for a patient having a stone in the ureter. A laborer having a calculus lodged in the upper ureter and progressing downward very slowly, or having periods in which the calculus remains stationary, who has repeated attacks of colic necessitating confinement to the home, frequently may be restored to his gainful occupation by surgical intervention at an earlier period than if expectant treatment is advised until the stone is in the lower third of the ureter. In like manner, individuals whose occupations require considerable expenditure of energy which provokes an attack of colic, because of their possibility of losing employment due to the frequent disability and financial status, may require more immediate relief.

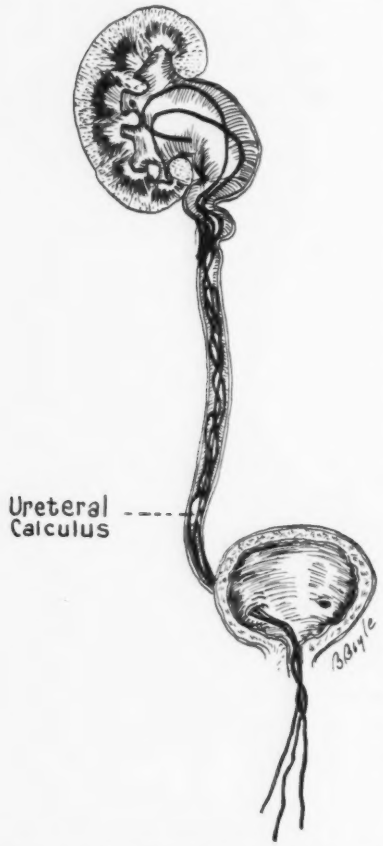

FIG. 2.—Multiple catheters utilized in removing a stone from the lower ureter.

(2) *Size of the Calculus.*—As a general rule the larger the calculus the less likely it is to pass spontaneously, and the more frequent will manipulative efforts fail. Obviously, the size of the ureter is of considerable importance with relation to the size of the calculus in determining the progress of the stone.

In Joly's[4] experience, patients passing stones at varying intervals of time are able to expel progressively larger stones from the ureter. Hinman[5] states that, generally speaking, stones of more than 1 cm. in size in the upper ureter, or more than 2 cm. in size in the lower ureter, require operation if they have not been affected by one or two manipulations, or if they have not moved for some time.

In this series it was noted that calculi larger than 1 cm. in diameter infrequently pass down the ureter spontaneously. In the absence of back pressure they may be observed and followed by roentgenographic studies.

The majority of ureteral calculi are small, however, and unless impaction is present or they are attached to the mucosa of the ureter by spicules, they will descend to the lower third of the ureter where, in the absence of complications or contraindications, manipulative efforts may be attempted.

(3) *Position of the Calculus in the Ureter.*—A stone in the lower third of the ureter usually is more amenable to manipulative efforts than a calculus in the upper ureter. Where a small calculus is present in the upper or middle third of the ureter, in the absence of complications, it is preferable to permit

the stone to descend to the lower third of the ureter before attempting manipulative procedures.

If the stone is over 1 cm. in size and has been in the upper ureter, for some time, and remains impacted or moves very slowly, operation is advisable. This is especially true in the presence of infection or increase in hydronephrosis. In some instances only a mild degree of obstruction is present as the urine passes by the irregularities in the calculus, thus producing slight dilatation of the ureter above the stone. This dilatation, however, may be sufficient to dislodge the calculus, which then passes into the pelvic ureter. In many instances a stone at this site is treated expectantly or by various manipulative efforts when surgical intervention should have been employed without hesitancy. The mortality is extremely low and the kidney is saved from the ravages of back pressure and infection.

In contrast to stones in the upper ureter, when they occupy a position in the lower third of the ureter, expectancy and manipulative efforts in the absence of contraindications are to be favored. Careful observation is essential, however, as they may remain here for some time, producing but few symptoms or only varying degrees of colic. However, surgical intervention should not be delayed following disappointment in the expectant or manipulative treatment.

(4) *Status of the Kidney Above the Stone.*—Continuous evidence of renal changes from back pressure or infection, as evidenced by pain over the kidney, or a progressively enlarging hydronephrosis, as revealed by an intravenous urogram, contraindicates continued conservative manipulative efforts. In like manner, if the urogram reveals that the calculus is producing complete blockage of the ureter, even in the absence of pain, the obstruction must be relieved. If a catheter cannot be passed beyond the stone, surgical intervention is advisable. In cases in which the pelvis of the kidney and calices are not visualized by intravenous urography, it does not imply that a normal or fairly normal function will not be revealed when the obstruction is removed. Joly states that the presence of a coexisting chronic parenchymatous nephritis contraindicates conservative medical management, this condition preventing the forcing of fluids.

(5) *Age of the Patient.*—In elderly, debilitated, senile patients, repeated manipulative efforts frequently are not well tolerated and may be attended by severe general reactions. In the presence of an enlarged prostate, cystoscopic manipulation is more difficult and is attended by considerable trauma. This condition may favor an open operation, although the calculus is of a size that manipulative treatment would be employed in a younger individual. In small children, manipulative efforts in selected cases may be employed. Newer instruments have been introduced in recent years to facilitate carrying out such procedures without trauma or difficulty. Again, however, recourse to surgical intervention should not be neglected in selected cases such as congenital anomalies which may render conservative procedures extremely difficult.

The presence of lesions in the opposite kidney, such as obstruction from various etiologic agents, stones, *etc.*, may influence the treatment to be recommended.

(6) *Coexisting Pathologic Conditions.*—Various other factors may influence recommending surgical intervention. The presence of a large cystocele, stricture of the urethra, fibroid uteri, and pelvic tumors, may contraindicate manipulative efforts. In the presence of anuria, the presence of a solitary kidney or bilateral ureteral calculi must be considered. Here we are confronted with an emergency and, if possible, the passage of a catheter beyond the obstruction is of paramount importance in facilitating urinary drainage, the immediate attack upon the calculus being delayed until the crisis is passed.

Manipulative Procedures.—In recent years urologic surgeons have been more enthusiastic regarding the manipulative management of ureteral calculi. There are several objectives to instrumentation, and the instrument to be employed is influenced by the purpose of the procedure:

(1) Drainage by passing a catheter beyond the stone to relieve back pressure and to assist in eradicating infection.

(2) Dilatation of the ureter:

(a) Passing a ureteral catheter or catheters beyond the stone and leaving them *in situ* for from 24 hours to three or five days (Fig. 2).

(b) Employing bulb catheters of varying sizes.

(c) Using mechanical dilators, such as the Dourmashkin bag, to dilate the ureter or the orifice below the stone.

(3) Using especially designed instruments for extraction of the stone or extractors, such as the Council, Welland, Howard, or Johnson.

(4) Meatotomy by fulguration or the use of especially designed ureteral scissors.

The large number of instruments available today for the manipulation of stones in the ureter attest to the fact that no single instrument or method is suitable in all instances.

Undoubtedly, experience with the various procedures influences the advisability and the selection of the instrument to be used in a given case.

As has been frequently stated, the manipulation of stones in the ureter is not an office procedure and hospitalization is to be recommended in all cases.

Many types of manipulative procedures are advocated by various authors. I still prefer the use of multiple catheters, and then the Council extractor if the stone is not delivered by means of catheters. The spiral dislodger is especially efficacious in the removal of calculi impacted in the ureteral meatus (Fig. 3). Larger stones lodged in the intramural portion of the ureter may be removed by employing fulguration or especially devised ureteral scissors (Fig. 4). Care and gentleness during manipulation, in order to minimize trauma of the ureter, are important.

After the cystoscopic removal of a ureteral calculus, a ureteral catheter is passed to the kidney pelvis to remain for a period of from 24 to 48 hours. This minimizes the incidence of pain following manipulative procedures.

In a series of 199 cases of ureteral calculi, reviewed a few years ago, it was noted that in 15 cases, or 7.9 per cent, the stone passed spontaneously; in 69, or 34.7 per cent, the calculus was expelled after cystoscopic manipulation

with multiple catheters; and 12, or 6 per cent, were extracted from the ureteral orifice. In 21 instances surgical intervention was required after manipulative efforts were unsuccessful. In 65 patients, or 32.7 per cent, surgical intervention

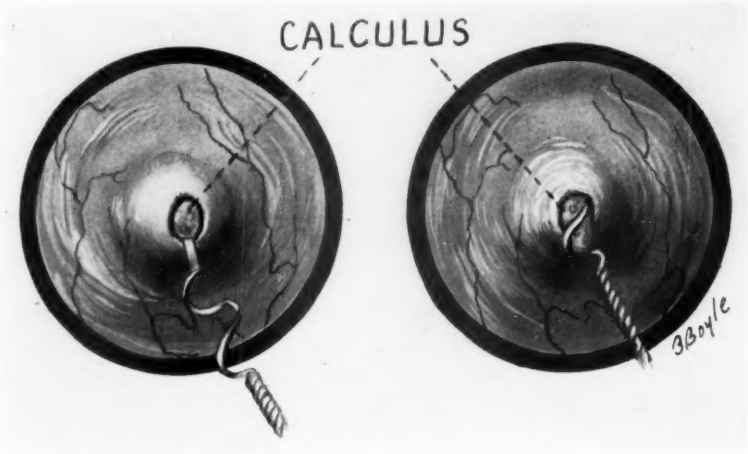

FIG. 3.—Spiral dislodger for removing stones from the ureteral orifice.

was advocated primarily, while in 17 patients operation was recommended but refused by the patient.

In a later series of 251 cases, it was noted that 43, or 17.1 per cent, passed the calculus spontaneously; 171, or 68.4 per cent were removed by surgical intervention; and 37, or 14.7 per cent, were removed by manipulation.

FIG. 4.—Incision in the lower ureter with cystoscopic scissors, for removal of a stone impacted in the lower end of the ureter.

In the present series of 350 cases, 66, or 18.9 per cent, passed the stone spontaneously; in 56, or 16 per cent, the calculus passed after manipulation; while in 228 cases, or 65.1 per cent, surgical intervention was deemed advisable.

From these statistics it is evident that there has been a gradual increase in the number of stones expelled spontaneously or by manipulative procedures.

In a series reviewed by Bumpus and Scholl,[6] at the Mayo Clinic, 72.7 per cent were removed by open operation, and 27.2 per cent by manipulative procedures.

The high incidence of surgical intervention in the present series may be accounted for by the relatively larger number of stones present in the upper ureter, and the fact that in many instances repeated manipulative procedures had been attempted before the patient entered the clinic, and further manipulative attempts to deliver the stone were not advisable.

In advocating manipulative procedures for the removal of stones from the ureter, the following must be considered: The economic status of the patient, the age of the patient, the size and position of the calculus, coexisting pathology rendering manipulative procedures difficult or hazardous, evidence that the patient does not tolerate cystoscopic procedures such as the development of pyelonephritis following instrumentation, the status of the kidney above the stone, the status of the opposite kidney, a fixed stone or one that has recently passed into the ureter, a stone complicated by a pronounced periureteral reaction usually associated with a fixed stone, in the presence of a progressively enlarging hydronephrosis, with or without infection, when repeated manipulative efforts fail, and certain congenital abnormalities.

Certainly, a dogmatic statement should be avoided as instances may arise in which each of these objections are not tenable.

Surgical Intervention.—The operative removal of a calculus from the ureter may constitute but one phase in the management of this group of patients. The status of the kidney above the stone must be given due consideration, as it may be damaged by back pressure and infection to such an extent that its potential ability to repair is *nil*. If the kidney is pyonephrotic, a nephrectomy is necessary; if a large dilated ureter also is evident, an additional ureterectomy may be advisable. With varying degrees of hydronephrosis conservatism is advisable unless functional studies show irreparable kidney damage.

In many instances the status of the kidney may be determined by intravenous urographic studies, or if a catheter can be passed beyond the stone functional studies and a retrograde pyelogram give the desired information. However, I have seen numerous cases with hydronephrosis associated with ureteral calculi which diminished markedly in size and the function returned to normal, or approximately normal, after removal of the stone. In all instances conservatism is the procedure of choice, if it may be safely recommended.

In recent years, refinement in the operative technic has diminished the period of hospitalization, the mortality, and morbidity in the group of patients in whom ureterolithotomy has been performed. A muscle-splitting operation and an extraperitoneal approach is utilized in removing stones in every portion of the ureter. This lessens the incidence of hernia and in many instances the patient may leave the hospital in seven to nine days after surgical intervention has been instituted.

In removing a calculus from the ureter I prefer to make the incision in the ureter slightly above the point of obstruction rather than directly over the

stone itself. This minimizes trauma to the ureteral tissue overlying the calculus which is already the site of a periureteritis. A forceps is passed gently down to the stone which is easily withdrawn. This decreases the incidence of stricture formation postoperatively.

The incision in the ureteral wall is reapproximated with No. 000 plain catgut sutures, avoiding passing through the mucosa of the ureter. A rubber tissue drain is introduced in all cases.

There is one operative procedure for the removal of a calculus from the lower ureter in women which, I do not believe, has received sufficient attention. This is the employment of vaginal ureterolithotomy. If a calculus can be palpated in the ureter upon vaginal examination, it may be removed readily by this route. This procedure has been employed successfully in 13 patients in this series, with no complications. While it has been stated that a fistula may result, this has not been our experience in any patient in this group.

In the present series of 228 cases, in which surgical intervention was necessary and ureterolithotomy was employed, four deaths occurred. One patient died of peritonitis, one of postoperative pneumonia, one from cardiac failure, and one patient succumbed from a cerebral embolism. In one instance a persistent ureteral fistula occurred, later requiring nephrectomy.

Complications are avoided by adequate preoperative study and postoperative care. The operative procedure *per se* is but one phase in the management of this group of patients. Intensive preoperative study and a well planned postoperative regimen cannot be overemphasized.

CONCLUSIONS

A study of the etiologic factors associated with calculous formation is essential in every patient with a ureteral stone.

A critical evaluation of the procedures available for the removal of a calculus from the ureter must be made in each individual case.

The indications for surgical intervention must not be overlooked and, because of the low mortality and morbidity, should be advised in indicated cases.

Experience with the various procedures available for the removal of a stone from the ureter influences the choice of method or instrument.

The treatment to be recommended is that which, in the experience of the surgeon, has been accompanied by the most satisfactory end-result.

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MALIGNANT TUMORS DEVELOPING IN SACROCOCCYGEAL TERATOMATA

HERMANN LISCO, M.D.*

BALTIMORE, MD.

FROM THE DEPARTMENT OF PATHOLOGY, THE JOHNS HOPKINS MEDICAL SCHOOL AND HOSPITAL, BALTIMORE, MD.

CONGENITAL MALFORMATIONS and tumors designated as dermoids or teratomata have for centuries greatly impressed and stimulated investigations by many students of biologic and medical problems. The literature dealing with various aspects of the sacrococcygeal group of teratomata alone is so voluminous that no attempt can be made to review it in this paper, nor is it feasible to discuss the various classifications or the theories concerning the nature and embryologic genesis of teratomata. Recent reviews of the subject are those of Ewing,[1] and MacCallum.[2] The latter presents a detailed and critical discussion of the theories of origin and many references to the original literature are given.

TABLE I

TEN CASES OF MALIGNANT DEGENERATION OF TERATOMATA
From the Literature

No.	Author	Year	Sex	Age at Time of Death	Type of Malignant Tumor	Metastases	Autopsy
	Certain Cases						
1	Rudolphy[4]	1897	♀	12 months	Papillary adenocarcinoma	Lungs	Yes
2	Fletcher and Waring[5]	1900	♂	29 months	Adenocarcinoma	Lymph nodes	Yes
3	Hinterstoisser[6]	1908	♀	23 months	"Alveolar sarcoma"	Lungs Liver Lymph nodes	Yes
4	Bergmann[7]	1911	♂	17 months	Papillary adenocarcinoma	Lungs	Yes
5	Stewart, Alter and Craig[8]	1930	♂	3 years, 3 mos.	Papillary adenocarcinoma	Lungs Liver Lymph nodes	Yes
6	Renner and Goodsitt[9]	1935	♀	11 months	Carcinoma	Invasion of rectum	Yes
7	DeVeer and Browder[10]	1937	♂	21 months	Embryonal carcinoma	Lymph nodes	Yes
	Probable Cases						
8	Gramm[12]	1902	♀	21 months	"Chondrosarcoma"	Lungs Lymph nodes	Yes
9	Pandalai, Forsyth and Stewart[11]	1924	♂	12 months	Papillary adenocarcinoma	?	None
10	Susuki[13]	1936	♂	3 years	Adenocarcinoma	Lungs Liver Lymph nodes	Yes

The histologic structure of sacrococcygeal teratomata has been carefully analyzed and described. The unusual nature and behavior of these growths is undoubtedly responsible for the great number of publications, which is entirely out of proportion to the frequency with which these tumors occur.

* Now at the Dept. of Pathology, Harvard Medical School, Boston, Mass.

Minor variations and insignificant peculiarities are added in some of the case reports of recent date, while other papers are devoted to considerations of the treatment of these tumors. Treatment, indeed, currently represents the major part of the problem of sacrococcygeal teratoma.

Malignant tumors developing in sacrococcygeal teratomata have occasionally been observed. The extreme rarity of such changes and the presence in our files of two cases showing the development of malignancy prompt this report.

An effort has been made to establish the actual number of similar cases in the literature (Table I). Several instances of alleged malignancy, and cited as such, have been omitted from this list on account of insufficient description or apparent faulty interpretation. This refers particularly to cases published in the latter part of the last and early part of this century.

CASE REPORTS

Case 1.—History No. H.L.H. 98937: E. E. Y., a white, female baby, was first seen at the age of ten months. She was referred to the hospital by her local doctor with the diagnosis of a tumor of the right buttock. This was present at birth and had slowly increased in size ever since.

Family History.—This was negative except for the occurrence of frequent tumors on the maternal side. Both parents are well.

Patient's History.—Birth was normal. On the day after birth the mother first noticed that the right buttock was slightly larger than the left. It slowly and progressively increased in size, especially during the eighth and ninth months. The buttock was always firm and at times warm. The anal opening was dislocated toward the vagina. Bowel movements had been quite normal.

Two months ago the child refused to sit or to lie on the right side. The appetite became poor, but there was no loss of weight. A diagnosis of a tumor of the right buttock was made and confirmed roentgenologically. An operation was advised, and the child was transferred to the Harriet Lane Home of the Johns Hopkins Hospital.

Physical Examination.—The patient was a ten-months'-old well-developed and well-nourished white female baby, that was extremely irritable and cried when made to sit up or to lie on the back. The baby preferred the knee-chest position and was standing on a wide base. There was marked lordosis. Both buttocks were quite prominent. The right buttock was larger than the left. There was a large, firm and smooth downward-projecting mass in the right buttock. The overlying skin was quite warm and there were dilated veins on the surface. Dilated vessels were also seen in the skin over the lower lumbar spine and the sacrum. There was also some slight yellowish pigmentation of the skin over this area and a mild depression could be seen over the sacral spine which was covered by a slight growth of hair. The sacrum seemed to be pushed backward. The rectum, on digital examination, was found to be pushed over to the left by a smooth, firm, rounded mass in the right side of the pelvis. The posterior vaginal wall was pushed forward slightly into the vaginal cavity. Behind it, a firm mass could be felt in the pelvis. The anal opening was wide and there was prolapse of rectal mucosa. About the anus a ring of bluish discolored skin about 3 cm. in diameter was seen.

The abdomen was somewhat protuberant. No masses could be felt anywhere in the abdomen. A few axillary, cervical and inguinal lymph nodes were palpable but not enlarged. A diagnosis of sacrococcygeal teratoma was made. The roentgenograms confirmed the diagnosis of a large tumor, seemingly arising from the region of the pelvic outlet. Collections of calcium deposits were seen in it. It was thought that these might represent teeth. Laboratory data were negative.

On surgical consultation, it was decided to irradiate the tumor before operation in order to reduce, if possible, the size of the tumor. From October 16, 1936, to November 9, 20 roentgen treatments were given. Half of these were directed to either side of the tumor. The distance was 50 cm.; a 2 Mm. Cu. and a 1 Mm. Al. filter were used, with 200 K. V., 20 Ma., a total of 1,740 r. in all was given in the course of this treatment.

The growth of the tumor seemed to come to a standstill, whereas it had been increasing in size before treatment. The patient tolerated these irradiations well. Twice there was a transient diarrhea.

The patient was discharged in good general condition, and was to be followed further in the dispensary. Just before discharge a soft cystic mass was felt at the dividing line between the two buttocks.

About three months later, at 15 months of age, the patient was admitted again. She had had a persistent upper respiratory infection while at home. Otherwise, she had been well until six days before admission, when it was thought that the tumor was growing again. At this time several areas of fluctuation were felt in the tumor, which now involved both buttocks, particularly the right.

During a period of 12 days, nine roentgen treatments were given. The dosages were as follows: 200 KV., 20 Ma., skin-target distance 50 cm., ½ Mm. Cu. and 1 Mm. Al. filters. A total of 792 r. was delivered. Five irradiations were directed toward the tumor from the left and four from the right side. There was no change in the tumor at that time, and the patient was again discharged for further observation in the Out-Patient Department. The child remained at home for three and one-half months. She received one treatment with radium in the second month (one month previous to her third admission).

Soon after the radium treatment the child became irritable and refused to stand or walk. She looked pale and lost weight. Two weeks before admission she developed obstinate constipation. She was admitted for the third time at the age of 19 months. The tumor had grown considerably larger and two soft lumps of large size had appeared on the surface of the mass. There was more distortion of the rectum and of the genitalia. Both legs were partially paralyzed and the muscles atrophied. In the right lower quadrant of the abdomen there was a firm mass projecting from the right pelvis and extending to the midline.

Operation.—June 18, 1937: Under general anesthesia, a large, partially firm and partially soft tumor was shelled out and dissected away from the bladder and the rectum. The tumor was found to extend up into the pelvis and was firmly attached to the coccyx, which was resected. The sacrum was curetted, since the tumor was attached to it also. A nodular mass of tumor was seen to extend up into the abdominal cavity and this could be removed also. The patient stood the operation well, and immediately postoperative had a formed stool. Several transfusions were administered. The operative wound drained and healed slowly.

After an initial improvement during the first three weeks after operation, an abdominal mass could be felt. It extended up to the umbilicus. Small ulcerations appeared about the rectum and the child became more and more cachectic. The abdominal mass increased rapidly in size and the liver became enlarged. The child died two months after the operation, at the age of 21 months.

Autopsy Report (No. 15448, Doctor McAllister). The description will be limited to points of particular interest.

The body is that of an extremely emaciated and dehydrated female baby. Many dilated veins are seen over the abdomen and over the back. There are several small shallow ulcers in the perineal region, and there is a draining sinus leading into the right buttock. There are a few palpable lymph nodes in each groin. Both buttocks are enlarged, the right being larger than the left. No other lesions are seen externally.

Gross Pathology.—A large tumor mass, situated in the retroperitoneal tissue pushes all the abdominal organs upward and anteriorly, including the aorta, the inferior vena cava,

and both ureters, which overlie this mass. The tumor measures approximately 13x13x2.5 cm. The right ureter is obstructed and the vena cava is dilated distally. The main tumor has eroded the vertebrae and intervertebral disks and the right ileum posteriorly. The tumor is soft, somewhat lobulated, and greyish-yellow. Several cysts are found in the tumor, the largest measuring 2.5 cm. in diameter. The tumor surrounds the vena cava and aorta. In the inferior vena cava there is, completely filling the lumen, soft yellowish material.

The entire region of vagina and ureteral orifices is infiltrated by the tumor. There is tumor material in the marrow of the head of the femur.

The large tumor is continuous with a smaller tumor in the right buttock. The draining sinus, mentioned earlier, communicates with this mass which is somewhat firmer and pink. The left buttock is free.

Many small nodules are found in both lungs and in the liver. These are of a greyish-white color and soft. The largest ones measure about 1.5 cm. in diameter. A mucoid material can be squeezed out of them. A few cystic areas are seen in some of them. Bronchial, periportal and retroperitoneal lymph nodes contain similar gelatinous tumor nodules.

The tumor removed at operation measures 12x10.5x10 cm. It is somewhat pear-shaped and surrounded by, for the most part, a smooth fibrous capsule. Portions of fat, numerous adhesions and remains of muscle are seen on one side. The opposite side of the tumor is smaller. It is on this part of the tumor that most of the adhesions and muscle tissue are found, and it shall be referred to as the base. The tumor is rather soft and of a somewhat elastic consistency. When cut in numerous sections, the surfaces present a rather uniform picture—showing numerous cysts varying from a few millimeters to 3.5 cm. in diameter. Most of the cysts are thin-walled and transparent. Many contain a gelatinous tenacious bluish-grey opaque material. Groups of cysts are sometimes surrounded by a membrane of connective tissue, giving it a nodular appearance. Small areas of black pigmentation are occasionally seen in the tumor. A few calcified foci are encountered, but no teeth are found. The capsule of the mass varies in thickness from 3 to 1 cm. At the base and along one side of the tumor there is a slit-like separation of the capsule, dividing it into a parietal and visceral portion. The narrow elongated cavity contains a small amount of greasy material and a few hairs in places. The inner surface of this cavity is roughened here and there. The more solid tissue at the base shows some large areas of necrotic, friable material in close association with some of the cystic cavities.

Microscopic Examination.—The tumor removed at operation shows a dense partially hyalin capsule and a variety of tissues. There are derivatives of all three germ layers. The cysts are lined by ciliated and nonciliated cylindrical epithelium, resembling the mucosa of trachea. Some cysts are lined by squamous epithelium. Islands of squamous cells are often found in the cylindrical epithelium as well. Other cysts are lined by cuboidal or flat epithelium. Many mucous glands, with ducts, are present in the interstitial tissue. The lumina of many cysts are filled with a homogeneous somewhat pink-staining material. In addition, parts of the following structures are found in the tumor: Cartilage and bone, smooth muscle, pigment cells, intestinal mucosa, pancreas with islands of Langerhans, ovarian stroma with structures resembling follicles, choroid plexus, nervous tissue, epidermal epithelium with appendages. There are inflammatory cells in some parts of the tumor, and a sinus is found showing fresh granulation tissue in which a few giant cells are seen.

Sections from the base of the tumor show an entirely different type of tissue in addition to the above-mentioned structures. It is composed wholly of a single-type of cell which has large polygonal and relatively pale-staining nuclei with little chromatin and but scant cytoplasm. In some regions the cytoplasm of the tumor cells is vaculated. The cells grow in single layers or in massed sheets. They are situated on a delicate vascularized network of connective tissue. Numerous papillary proliferations are seen and the tissue has, on the whole, the characteristic appearance of a papillomatous tumor. In some

areas an acinar structure is noted. Here a pink-staining, homogeneous material is often found in the lumina, formed by the tumor cells.

The number of mitotic figures varies considerably. In focal areas tumor cells are compactly clustered and in other areas the structure is loose. There are foci of necrosis and hemorrhage. There is invasion of adjacent tissues and blood vessels.

It is this tumor which has invaded the bones and retroperitoneal tissues. There is a thrombus of tumor cells in a branch of the left external iliac vein. The metastases in the liver and lung show the same type of tumor cell. Other microscopic studies revealed a chronic cystitis and an acute necrotizing pyelitis of the right kidney.

Anatomic Diagnosis: Congenital coccygeal teratoma, involving right buttock. Papillary adenocarcinoma arising in teratoma and invading right buttock, lower lumbar and sacral vertebrae, right ileum and head of femur. Extension of tumor into pelvic and retroperitoneal tissues. Metastases in liver, lungs, retroperitoneal and bronchial lymph nodes. Urethral and ureteral obstruction by tumor. Chronic cystitis. Chronic and acute necrotizing pyelitis, right. Compression and invasion of pelvic veins and inferior vena cava. Draining sinus communicating with tumor mass in right buttock. History of preoperative roentgenotherapy and radium treatment.

Case 2.—History No. 3822: H. E. B., white, male, age 13 months, was admitted to the Johns Hopkins Hospital, April 12, 1926, because of constipation and anuria.

Family History.—Not remarkable.

Patient's History.—Patient was a full-term child. At the time of birth a small reddish discoloration was noticed just to the left of the coccyx on the thigh. This resembled a birth mark. It measured about 1.5 cm. in diameter. The family physician advised no treatment. At the age of two or three months a small lump of walnut-size was found in addition to the discoloration. Neither the discoloration nor the lump seemed to increase in size during the first four or five months of life. A little later the mother thought that the area of discoloration and the mass beneath it increased in size. The attention of the family physician was called to this but he advised against any interference. The child developed some slight constipation at the age of about nine months. Since the child was given solid food for the first time during this period, it was thought that the constipation was due to the change of food. The constipation persisted, however, and became worse slowly, so that at the age of 12 months, enemas had to be given. A doctor was again consulted and he gave calomel, whereupon the bowels moved freely, though for a short time only.

A week later it was noted that the left leg was somewhat swollen. The area of discoloration and the mass beneath were larger than before, and there were dilated blood vessels in the skin above and around it. The child lately assumed a knee-chest position when awake and seemed to be much more comfortable in this position.

One week before admission, at the age 13 months, the child seemed toxic and was passing very small amounts of urine. Catheterization was performed, and the child was relieved. Repeated catheterization became necessary, which procedure became more and more difficult. As the symptoms of constipation and anuria became worse, and catheterization more difficult, it was decided to hospitalize the child.

When the patient entered the hospital he had not voided for several hours, and the bladder was greatly distended. A retention catheter was introduced and a decompression apparatus used. The retention was relieved, and the child started voiding again in about one week.

Physical Examination.—The patient was a slightly under-developed, weak and irritable child. The abdomen was distended. The bladder dulness extended two fingers' breadth below the umbilicus. On the left buttock, to the left, and close to the sacrum and coccyx, there was a subcutaneous, soft mass covered by bluish discolored skin, measuring about 3 cm. in diameter. It was freely movable, but seemed to be attached to the deeper structures of the sacrum. The superficial veins of the skin were dilated. The left thigh was swollen. On suprapubic palpation an indefinite mass could be felt along-

side the distended bladder. On rectal examination an almost complete obstruction of the rectum was found in the ampulla. A slit-like opening was all that remained of the rectal canal. The rectal mucosa was smooth and intact everywhere. A large tumor mass could be felt; this was firm and filled out the concavity of the sacrum and was attached to both sides of the pelvis. The mass was so firm as to suggest bone formation. Roentgenologically, a distortion of the lower portion of the sacrum was noticed.

A diagnosis of tumor of the pelvis was made, with the probability of a periosteal sarcoma. Hence, roentgen and radium treatment seemed most advisable. This combined treatment was carried out during the following weeks. The roentgenotherapy was continued for 18 days, beginning at a dosage of 15 minutes and gradually increasing up to 20 minutes. He was given a total of five half-hour radium treatments per rectum, making a total of 500 mc. hours.

A few days after entering the hospital the left thigh was noticed to be swollen and there was definite swelling of the left inguinal nodes. The right inguinal nodes were normal in size.

The treatment was well-tolerated, and the tumor mass became much smaller. The intestinal and urinary obstruction disappeared almost completely. The patient was able to void and normal stools were passed. The swelling of the left thigh and the discoloration of the skin had disappeared, and the subjacent tumor mass had decreased to about one-half the size noted on admission. The patient was discharged 19 days after admission.

For two weeks, roentgenotherapy was continued three times a week. The child improved steadily and continued to do well for about one month. Reexamination, in about four weeks after discharge from the hospital, showed a fairly well-nourished child. An indefinite mass could still be felt on palpation to the left of the midline in the pelvis. The mass had decreased in size considerably. The enlarged lymph node in the left groin had entirely disappeared. The left thigh was still a little larger than the right. The mass in the upper portion of the left buttock was still present but it was much smaller and softer than before.

The general improvement of the child lasted for about one month. After this time the tumor began to grow rapidly. Urinary obstruction occurred again.

On June 1, 1926, two months after the final admission, the tumor had spread to the inguinal nodes on the left side and also the right side. Small nodular masses could be felt in the abdomen and in the liver. The tumor at the coccyx had not increased in size. Roentgenograms showed metastases also in the lungs. The child became weaker, and finally died, July 26, 1926, almost four months after the final admission.

Autopsy Report (No. 9375, Doctor Forbus). The report will be limited to the points of interest. (Abdominal incision only.)

The body is that of an emaciated male child, 16 months of age. The abdomen is greatly swollen. The lower extremities are edematous, the left leg more so than the right. Both buttocks are quite prominent. Just to the left of the tip of the coccyx, and extending for about 5 cm. up over the posterior surface of the sacrum, there is a soft cyst-like mass. The overlying skin is of a bluish color.

The abdominal organs are greatly distorted in shape and location, due to the presence of extensive nodular masses. In the pelvis, occupying the retroperitoneal tissues, there is a large tumor mass which completely fills the whole cavity. This has pushed aside all the pelvic organs. The bladder is pushed far upward, in such a way that it rests on the anterior surface of the tumor mass, right above the brim of the pelvis. In attempting to remove the tumor, after a dissection of the pelvic organs which are not involved by it, it is found that there is a direct continuation of tumor tissue into the structures of the left thigh beneath the inguinal ligament. The tumor is very densely attached to the floor of the pelvis and to the anterior surface of the sacrum and coccyx. There is no invasion of any bony structures. There is a distinct continuity between this tumor and the cystic tumor which was described as being located in the sacral region externally. It is easy to remove the sacral cystic tumor from its bed.

The branches of the vena cava inferior are markedly compressed by tumor masses and a thrombus is found in the main stem of the inferior vena cava. There is an ulceration of the mucosa of the rectum. The retroperitoneal tissues and lymph nodes are diffusely invaded and replaced by a rather soft yellowish-grey, brittle tissue which is of a tenacious and mucinous character. There are widespread hemorrhages. There are numerous metastases in the liver, the lungs, and in bronchial lymph nodes. The better preserved, smaller metastases show a homogeneous grey, granular surface with some mucoid material. There is tumor tissue in branches of the portal veins also.

The pelvis of each kidney is somewhat dilated but there is no appreciable dilatation of the ureters. The other organs show no lesions.

Frozen-section of the sacral tumor show a variety of tissues including intestinal mucosa, skin, and nervous tissue. Sections of the invading tumor show a different type of tissue, which will be described later.

The sections which remain for study (other sections and blocks have unfortunately been lost) show the following: The tumor mass, located subcutaneously in the left buttock, shows a single cyst lined by squamous epithelium. Sections from the cystic part of the pelvic tumor show cysts lined by high columnar mucus-producing epithelium. The epithelium sometimes changes in character from place to place. In some places it is squamous, in others ciliated, in again others it is cuboidal. A few hair follicles are seen in the cysts lined by squamous epithelium. These cysts are surrounded by a rather dense connective tissue. An island of undifferentiated epithelial tissue is found in the interstitial tissue. Smooth muscle as well as nervous tissue is seen.

The malignant tumor is composed of different cells. These cells are somewhat cuboidal; they have little cytoplasm and consist for the most part of large polygonal nuclei with varying amounts of chromatin. The nuclei are relatively pale. These tumor cells are arranged in various ways: They tend to grow in single layers along fine strands of connective tissue, forming small papillary branching structures. In other places they grow in solid columns and in others small acini are formed by tumor cells. Solid nodules of tumor cells are found here and there, surrounded by connective tissue membranes. A cystic appearance is frequently seen and in these parts a pale bluish, homogeneous substance lies between loosely arranged tumor cells. Many mitotic figures are seen. There are necroses and hemorrhages. The metastases throughout the body show the same type of cell and the same variations in arrangement, which is predominantly that of a papillary adenocarcinoma.

The remaining organs show no lesions except for a chronic ulceration of the mucosa of the rectum, which shows loss of mucosa and granulation tissue with an occasional giant cell.

Anatomic Diagnosis: Papillary adenocarcinoma arising in cystic sacrococcygeal teratoma. Extension of tumor into pelvic and retroperitoneal tissues and left thigh. Metastases in liver and lungs, retroperitoneal and bronchial lymph nodes. History of repeated urinary and intestinal obstruction by pelvic tumor and of deep roentgen and radium treatment, with relief of symptoms. Pigmentation of skin. Ulceration of rectum. Slight obstruction of both ureters and slight hydronephrosis, bilateral. Thrombosis of inferior vena cava.

Discussion.—Both cases represent typical congenital sacrococcygeal teratomata. They were both found at, or soon after birth. Derivatives of all three germ layers were found in both tumors.

The outstanding feature in these two cases is the development of a malignant tumor in the teratoma. Both tumors had infiltrated the adjacent tissues and metastasized to various organs. They showed very striking similarities in structure (Figs. 1 and 2).

It has been pointed out by several authors that teratomata—wherever

they occur—are a potential source for the origin of a malignant tumor. MacCallum[2] states: "While it is true that the teratoma itself is benign, it is not at all uncommon to find the development of a distinct carcinoma at some point in its epithelium, exactly as we find it in the body in general." As a rule, one type of cell only assumes the malignant character and spreads throughout the body. The possibility that a variety of cells in a teratoma are stirred to such

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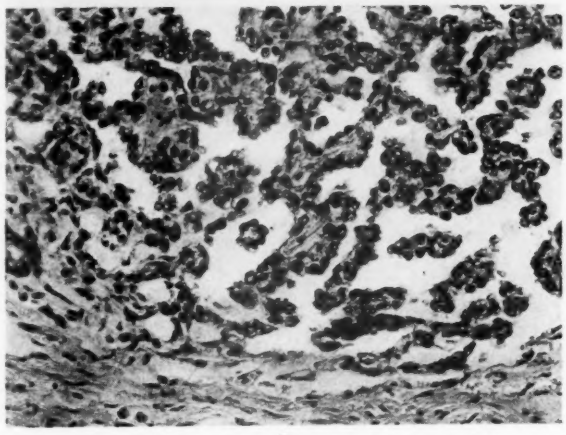


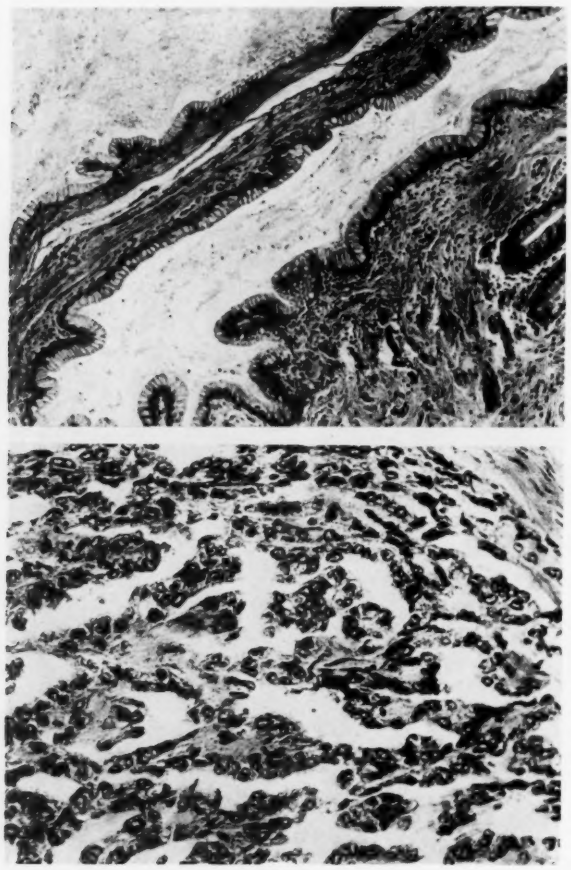
B

FIG. 1.—Case 1: Path. No. 15448. (A) Portion of teratoma. (B) Portion of papillary adenocarcinoma.

a change and that combinations of tissue metastasize is remote, and has not been shown to occur. However, Schairer[3] reports a remarkable case of a 14-year-old girl who had a teratoma of the left ovary. This was composed of mature and immature tissue elements of all three germ layers. In addition, a very immature and unclassifiable type of tissue was seen in it. There were numerous metastases and in these all tissues of the original tumor were found. The immature cell-forms predominated in the metastases. As it is unlikely

that tissue complexes became malignant and metastasized, as pointed out above, the author explains his case by assuming that a part of the very undifferentiated multipotential portion of the teratoma became malignant. These cells were then swept away by either the blood or lymph stream or implanted themselves on the peritoneum. Here, a number of them proceeded to differentiate and thus images of the original tumors were formed, containing

A



B

FIG. 2.—Case 2: Path. No. 9375. (A) Portion of teratoma. (B) Portion of papillary adenocarcinoma. (Photographs by Milton Nongl).

cysts, cartilage, and neuro-ectodermal tissues. It seems likely that in this case also only one type of cell was stimulated to malignant growth.

The cases reported herewith, and all those collected from the literature showed the development of malignancy, also, of only one type of cell. It is interesting, in this connection, to note the frequency of papillomatous adenocarcinomata. Moreover, all but two cases were malignant tumors of epithelial origin. The case of Hinterstoisser[6] can probably be interpreted, on account of

the minute description, as a carcinoma, while the exact nature of the tumor described by Gramm[13] remains obscure.

The first trustworthy report of a malignant tumor arising in a sacrococcygeal teratoma is that of Rudolphy.[4] The description of the original tumor, undoubtedly, characterizes it as a teratoma and the detailed report on the histology of the malignant tumor makes the diagnosis of a papillary adenocarcinoma certain. The case of Fletcher and Waring[5] also seems to be beyond doubt, judging from the clinical and pathologic data. In Hinterstoisser's[6] case a teratoma was described containing cystic cavities, bone and cartilage, and also some structures which were referred to as round cell sarcoma. The child was well for 21 months after operation, and then a pelvic tumor was found. At autopsy there was a large retroperitoneal mass with metastases in lymph nodes, lungs and liver. This was diagnosed as large cell alveolar sarcoma. It is likely, and the description suggests, that the author was dealing with an adenocarcinoma, although its identity cannot be ascertained today. The case of Bergmann[7] (No. 4 of his series) undoubtedly belongs in this series. No malignant changes were found in the teratoma removed at operation but four and one-half months later a large pelvic and retroperitoneal tumor and widespread metastases were found at autopsy. The tumor showed a papillary structure and gland formation. The case of Stewart, Alter and Craig[8] is a typical congenital sacrococcygeal teratoma in which a papillary adenocarcinoma developed. There were metastases in liver, lungs and lymph nodes. In Renner and Goodsitt's[9] case a typical postsacral teratoma was found and removed at operation. Ten and one-half months later a second tumor had developed which was anterior to the sacrum. Both proved to be teratomata, but in the second tumor a papillary tumor with attempts to gland formation was described in addition to the teratomatous structure. There was invasion of the wall of the rectum. DeVeer and Browder[10] describe a sacrococcygeal teratoma in a six-months-old child. This was removed and no malignant changes were found. Fifteen months later the child died of a tumor, with local extension and metastases to lymph nodes. The tumor is described as embryonal carcinoma.

To these seven cases three more can be added, although they do not show as much evidence either of the true nature of the teratoma or of the malignant tumor.

The case of Pandalai, Forsyth and Stewart[11] is another example of a papillary adenocarcinoma, developing in a teratoma. The papillary adenoma and carcinoma are supposed to have shown striking resemblances to tumors of the choroid plexus. There was no autopsy. Susuki[12] in a paper on "Teratomata" describes an adenocarcinoma with widespread metastases originating in the left buttock. He fails to describe the teratoma. The clinical history is suggestive of the presence originally of a congenital teratoma. The case of Gramm[13] has been noted frequently as an example of this type of tumor. As the original paper was not obtainable it is impossible to include this case with any degree of certainty in this series. However, the data given

in other papers[6, 14] do indicate that there was a teratoma, and do suggest that there was a malignant tumor with metastases to the lungs and lymph nodes. It was diagnosed as chondrosarcoma.

Additional cases described as teratomata with malignancy and some of them cited as such as in the literature, are those of Frank,[15] Nakayama,[16] Leopold and Phillips,[17] Heigl,[18] Sawday,[19] Weintraub and Young,[20] and Gruber.[21] These cases have been referred to in an earlier paragraph and it may suffice to say that there seems no justification to include these cases in this list. There was either apparent misinterpretation of the nature of the malignant tumor or absence of any evidence of a teratomatous tumor. Metastases occurred in none of them, and some of the reports are too fragmentary to draw any conclusions (Table I).

COMMENTS.—It is well known that malignant tumors may arise in teratomata in other parts of the body. They occur, for instance, in such tumors of the testis, the ovary, or the mediastinum. The material presented in this paper clearly demonstrates the possibility of malignant degeneration in the group of sacrococcygeal teratomata. This potential danger should be borne in mind in all consideration of treatment. Law,[22] in a discussion of pelvic tumors with sacral attachments, advocates early treatment: "We believe that, owing to the demonstrated tendency to malignant degeneration, these tumors should be removed when recognized." Similar opinions have been voiced by Stewart, Alter and Craig,[8] and others. Irradiation as a palliative measure is undoubtedly indicated in all cases in which malignancy with metastases has ensued. The demonstrated recurrence in some cases and the development of malignancy even after early operation perhaps indicates the necessity of postoperative prophylactic irradiation even in the absence of malignant changes in the tumors removed at operation. Since some of the malignant tumors were found in the tissues at the base of these tumors (near the point of attachment to bone, connective tissue, or cartilage) it appears important to pay particular attention to this region in microscopic studies of operative specimens.

SUMMARY

(1) Two cases of typical congenital sacrococcygeal teratoma are reported. In each of them a papillary adenocarcinoma with widespread metastases developed.

(2) The literature is reviewed and ten similar cases have been found.

(3) The necessity of early surgical treatment is pointed out.

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STUDIES ON THE BLOOD HISTAMINE IN CASES OF BURNS *†

BRAM ROSE, M.D., PH.D.
AND
J. S. L. BROWNE, M.D., PH.D.
MONTREAL, CANADA

FROM THE MCGILL UNIVERSITY CLINIC, ROYAL VICTORIA HOSPITAL, MONTREAL, CANADA

ALTHOUGH a great amount of experimental work and clinical observation has been directed toward the solution of the etiology of shock in general, there still remains a divergence of opinion as to the actual factor or factors which may be responsible. Perhaps, as Blalock[1] notes in his recent monograph, there is more evidence in favor of the toxic theory in burn shock than in most other forms. This is borne out in part by the results of treatment which inhibits the absorption of toxins, such as the tannic acid method of Davidson.[2]

The possibility that some toxin might be liberated from burned tissue, and thus be responsible for the shock-like state which is sometimes observed in patients after burns, was considered early in the studies on this subject, and a great many possible agents have been named. Evidence in favor of the toxic theory is based mainly on the effect of transplanting the skin of burned to healthy animals, producing shock in the recipients and alleviating symptoms in the donor animals (Vogt,[3] Vaccarezza[4]), or on the effects of the injection of extracts from burned tissues into healthy animals (Robertson and Boyd[5]), or in the detection of a vasodepressor substance in the fluid perfusing a burned limb (Nagamitu[6]). Much of this work, however, has remained unconfirmed, and evidence against the toxic theory of burns has been presented by Harrison and Blalock[7] who were unable to note any effect on animals due to the transplantation of burned skin. Further evidence against this theory was provided by Harkins, Wilson and Stewart,[8] and Fender.[9] An excellent review and discussion has been given by Harkins.[10]

In the early experiments on histamine, Dale and Laidlaw[11] noted the marked similarity between the effects of a large dose of histamine and the symptoms of traumatic shock. They suggested that the absorption of histamine or some similar substance might be the cause of the symptoms of traumatic shock. As pointed out by Barsoum and Gaddum,[12] there is a marked similarity between the electrolyte and other changes of the blood in both conditions. Subsequent investigation, however, did not support this theory, principally because of the inability to demonstrate an accumulation of histamine in the blood of shocked animals (Smith[13]). Furthermore, the experiments of Dragstedt and Mead[14] showed that when histamine shock was produced in

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dogs, histamine could readily be found in the blood of these animals. On the other hand, using the same methods of detection, it was not possible to note an increase of the histamine content of the blood of dogs in traumatic shock. Thus, the histamine theory of shock was rejected by many workers, for it was thought that if histamine were responsible for the production of symptoms, it must be increased in the peripheral blood. As will be pointed out, this conception may be an erroneous one in the case of the human at least.

The first observations on the blood histamine after burns were made by Barsoum and Gaddum[12] shortly after their description of the method for the extraction of histamine in blood. Nine cases in all were investigated, four of which were described in detail. A marked increase in the blood histamine was noted after the fifth or sixth day following the burn, later than the usual time for the development of secondary shock. They felt, however, that there was some correlation between the area of the burn and the magnitude and duration of the rise in histamine but were of the opinion that there was no clear evidence of a correlation between the blood histamine and the clinical condition of the patient. Code and MacDonald[15] described an additional case of burns in whom the blood histamine was determined. Their findings agreed, in general, with those of Barsoum and Gaddum.[12]

In the present studies, seven cases were available. Six of these were burned at the same time, and three were admitted to the Royal Victoria Hospital within an hour of the accident. Three others were admitted to the Montreal General Hospital, and were not studied until the ninth day. A seventh case, previously described (Rose and Browne[16]) is included.

In all instances the histamine content of the blood was determined by the Code[17] modification of the Barsoum and Gaddum[18] method. Hemoglobin estimations were carried out using the Evelyn photo-electric colorimeter, and the plasma proteins were determined by the falling-drop apparatus, as recommended by Scudder.[19] Blood specimens were removed from the large vein on the outer aspect of the arm or from the antecubital vein when possible. Stasis was avoided by the removal of the tourniquet before withdrawing the blood and clotting was prevented by the placing of a small amount of heparin (Connaught Laboratories) in the syringes. In this manner, all the determinations could be made from the same specimen of blood. Hematocrit estimations were always carried out as an additional check on the hemoglobin, and as a means of obtaining the small amount of plasma necessary for the determination of the plasma proteins. All histamine determinations are expressed as *gamma* of base per 100 cc. of blood (*gamma*, or $\gamma = 0.001$ mg., or microgram).

Blood Histamine in Normal Patients.—In a previous communication (Rose and Browne[16]), histamine determinations were carried out on the blood of 50 normal persons. It was found the average histamine content of the blood is 4γ per 100 cc. with variations of from 2–7.5γ per 100 cc. It was noted, further, that the histamine level of the blood of any one individual remains remarkably constant over long periods of time. These findings agree, in general, with those of Barsoum and Gaddum,[18] and Code and MacDonald.[15]

EFFECT OF CUTANEOUS BURNS ON THE BLOOD HISTAMINE OF PATIENTS

Case 1.—Patient No. 289: This man was admitted to the hospital within one hour after sustaining severe burns about the face and neck, both hands and forearms, and the area about the elbows. His condition was considered fair. A specimen of blood was obtained and, under a general anesthesia, his wounds were cleansed and tannic acid was applied. He received an intravenous injection of 500 cc. of half plasma and saline. The details of treatment, along with the changes in the blood histamine, hemoglobin, plasma proteins and blood pressure are shown in Chart 1. It will be observed that there

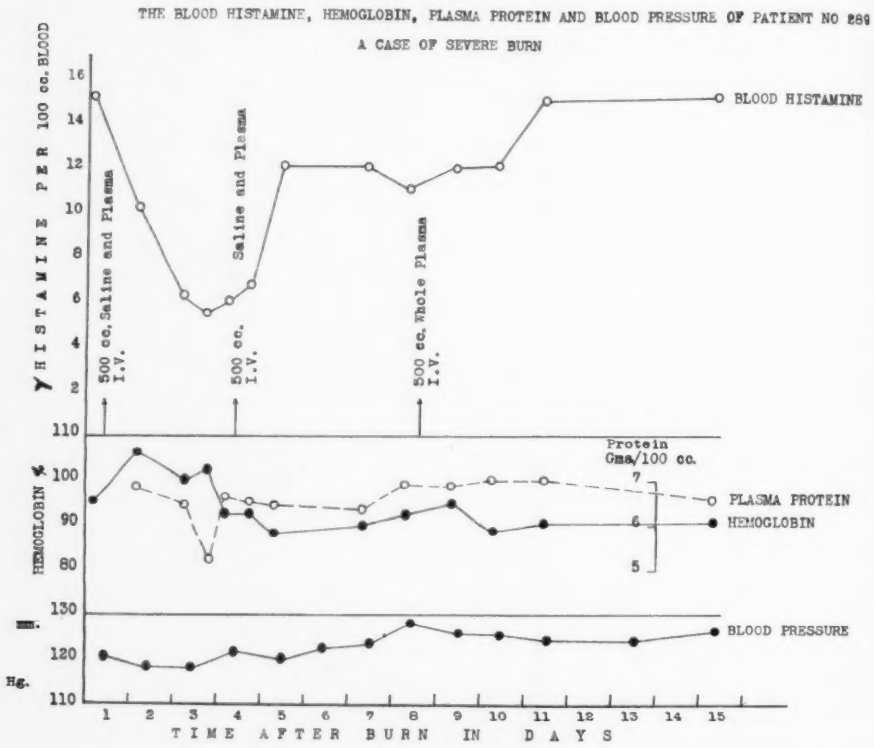
THE BLOOD HISTAMINE, HEMOGLOBIN, PLASMA PROTEIN AND BLOOD PRESSURE OF PATIENT NO 289
A CASE OF SEVERE BURN
γ HISTAMINE PER 100 cc. BLOOD
BLOOD HISTAMINE
500 cc. Saline and Plasma I.V.
Saline and Plasma
500 cc. I.V.
500 cc. Whole Plasma I.V.
HEMOGLOBIN %
Protein Gms/100 cc.
PLASMA PROTEIN
HEMOGLOBIN
BLOOD PRESSURE
TIME AFTER BURN IN DAYS

CHART 1.—Case 1: The blood histamine, plasma protein, hemoglobin and blood pressure are shown.

was little alteration in the hemoglobin and plasma protein, indicating that the intravenous therapy was adequate, and that hemoconcentration was being controlled. The blood histamine was high one hour after the burn, and it will be noticed that there was no indication of shock at this time. The blood histamine fell rapidly to a level of about 6γ per 100 cc. on the morning of the third day, where it remained for several days. At this time there was a moderate amount of edema, but the clinical condition of the patient was good. It will be noticed that there was a slight tendency to hemoconcentration at this time also. On the fifth day, as the patient began to improve clinically, the blood histamine had risen to a high level, reaching 15γ per 100 cc. on the eleventh day, where it remained until the twentieth day, when he was discharged.

Case 2.—Patient No. 290: A male, age 27, was admitted to the hospital one hour after sustaining very severe burns about the head, face and neck, upper chest and back, both hands, forearms and lower arms. His condition was considered to be serious and it was believed that part of the upper respiratory tract mucous membrane was also

damaged. A sample of blood was taken and, under a general anesthesia, the wounds were cleansed and tannic acid was applied. An intravenous injection of 500 cc. half plasma and saline was administered. On the following morning, there was beginning evidence of edema, and the patient was slightly toxic. Because the hemoglobin had risen to 114 per cent an intravenous injection of 1,000 cc. half saline and plasma was administered. Blood concentration was adequately controlled by the intravenous administration of plasma from this time, as indicated in Chart 2. Clinically, however, the patient was very

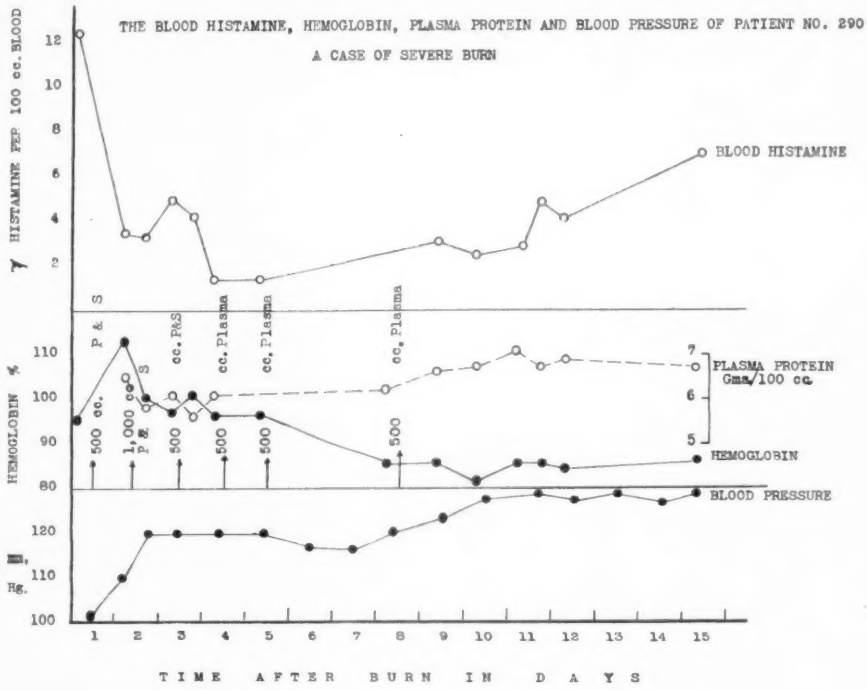

CHART 2.—Case 2: The blood histamine, plasma protein, hemoglobin and blood pressure are shown.

toxic and difficult to handle. The edema was very marked about the face and arms, beginning about 24 hours after the burn and increasing until the third day. It began to decrease about the seventh day and he improved slowly from that time on. It will be observed that as the toxemia and edema increased, the blood histamine declined until it was 1.5γ per 100 cc. on the morning of the fourth day. It was impossible to obtain blood on the sixth and seventh days. It will be seen that there is a definite correlation between the clinical condition and the histamine level of the blood. By the fifteenth day, the blood histamine had reached a level of 6.5γ per 100 cc. and the patient was discharged on the twenty-fifth day.

Case 3.—Patient No. 291: A male, age 45, was admitted to the hospital one hour after sustaining severe burns about the face, neck, both hands and the lower forearms. A specimen of blood was taken, and without anesthesia, the wounds were cleansed and saline dressings applied. His condition was considered good. On the following morning, although 2,700 cc. of fluid had been taken by mouth, the hemoglobin had risen to 130 per cent, indicating a marked reduction in plasma volume. The details are shown in Chart 3. He was given an additional 1,500 cc. of fluid by mouth during the day, and at 11 P.M. the hemoglobin had risen even further, to 138 per cent, and the hematocrit was 80. Thus, though the patient seemed in good condition clinically, marked hemoconcentration had

taken place. He was given 1,000 cc. of saline and plasma intravenously, and on the following morning (third day) the hemoglobin was still 118 per cent. By the administration of additional plasma it will be seen that the blood concentration was restored to within normal limits only by the evening of the fourth day. It will, furthermore, be noted that the blood histamine was not greatly increased to start with and fell rather rapidly after the third day to a very low level, 0.57 per cent 100 cc. by the morning of the fifth day. Up to this time, the patient had been well clinically, although there was

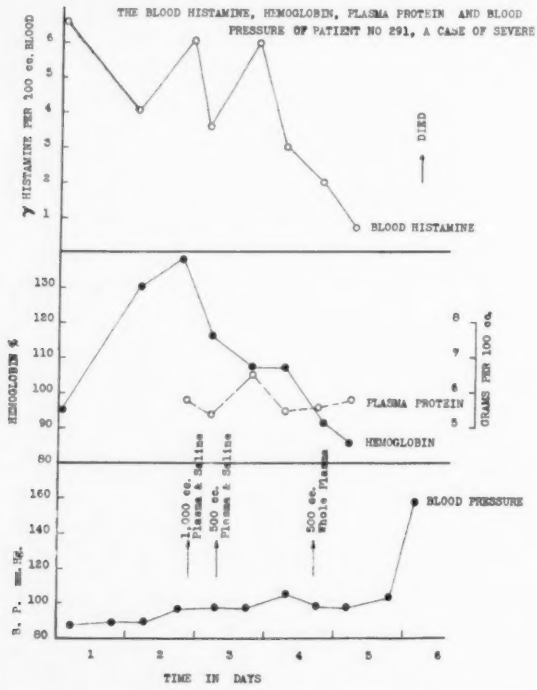
THE BLOOD HISTAMINE, HEMOGLOBIN, PLASMA PROTEIN AND BLOOD PRESSURE OF PATIENT NO 291, A CASE OF SEVERE BURN
γ HISTAMINE PER 100 cc. BLOOD
DIED
BLOOD HISTAMINE
HEMOGLOBIN %
GRAMS PER 100 cc.
PLASMA PROTEIN
HEMOGLOBIN
1,000 cc. Plasma & Saline
500 cc. Plasma & Saline
500 cc. Whole Plasma
BLOOD PRESSURE
B. P. mm. Hg.
TIME IN DAYS

CHART 3.—Case 3: The blood histamine, plasma protein, hemoglobin and blood pressure are shown.

some purulent discharge on the dressings. About 6 P.M. on the fifth day, he complained of feeling chilly, the temperature and pulse began to increase but the respirations were normal. At about 12.30 A.M. on the sixth day there was a sudden increase in the blood pressure from 100 to 160 Mm.Hg. The temperature was 105° F. and the pulse was about 140. He died suddenly at 2 A.M.

A postmortem examination was made 48 hours later. The burned areas were a bright red. The abdominal viscera appeared slightly pale. The liver, spleen and kidneys were normal in size and appearance. They did not drip blood on section. There was no evidence of ulceration throughout the gastro-intestinal tract. The adrenal glands showed no evidence of gross change and were of normal size. The heart and lungs were removed together. No evidence of a thrombus or embolus was found. The lungs were slightly hemorrhagic. Examination of the brain showed a small brown area about the size of a small pea in the pons. On microscopic section, however, this was found to be due to a localized dilatation of blood vessels and there was no actual hemorrhage. The cause of death was, therefore, not ascertained.

It was previously believed that a midbrain hemorrhage could be the cause of such a

death, but no such lesion was found. Thus, the only abnormal finding which was detectable 12 hours before death was the markedly diminished blood histamine.

Case 4.—A male, age 34, was admitted to the Montreal General Hospital with first degree burns about the face, neck and hands. There was also a small burned area on the left leg. Under a general anesthesia, his wounds were dressed with tannic acid and silver nitrate. His condition was good and he made a rapid recovery, being discharged on the fourteenth day. As will be noted in Chart 4 the blood histamine on the ninth and twelfth days was within normal limits.

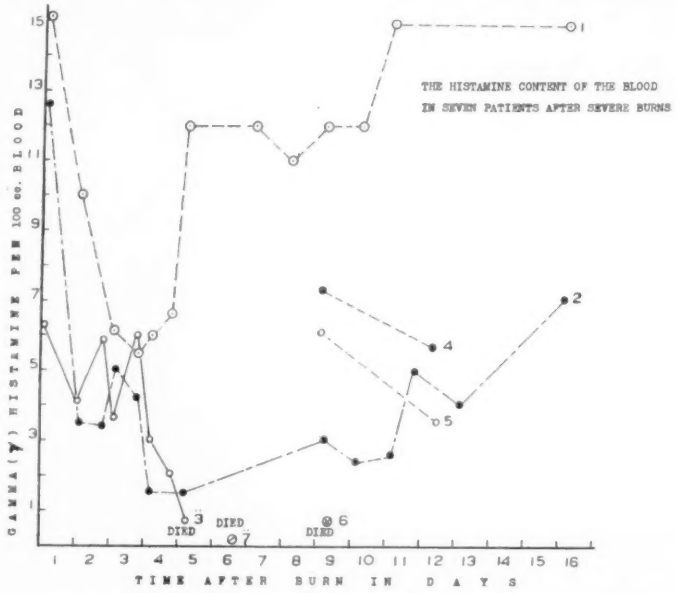

CHART 4.—This figure represents the histamine content of the blood of some cases of severe burns taken at various intervals. It will be noted that immediately following the burn the blood histamine is markedly increased in Cases 1 and 2. There is then a decrease in the blood histamine content of Cases 1, 2, and 3 at about the third and fourth days. This decrease is correlated with the signs of damage and the presence of edema. The blood histamine then decreases even further if the state becomes more severe, as in Cases 6 and 7, or increases as recovery ensues, as will be noted in Cases 1 and 2.

Case 5.—A male, age 45, was admitted to the Montreal General Hospital after sustaining third degree burns of the head, face, neck, both hands, wrists, forearms and two-thirds of the back. The burned areas were sprayed with gentian violet. The hematocrit reading was 54 on the day of admission and 61 on the second day. Histamine determinations were made on the ninth, twelfth and sixteenth days. It will be seen (Chart 4) that they were within normal limits. The hematocrit readings were 41, 41 and 39, respectively. He made a good recovery.

Case 6.—A male, age 34, was admitted to the Montreal General Hospital with first and second degree burns about the head, face, neck, left side of thorax, hands and forearms. Under a general anesthesia, tannic acid and silver nitrate were applied to the wounds. The urine contained albumin on the third day, and R. B. C. and casts appeared by the fifth. Anuria developed on the ninth day. The blood histamine was determined on the ninth day, and was found to be markedly decreased. The hemoglobin was 106 per cent, and the hematocrit was 48 (Chart 4). A transfusion of 500 cc. was given on the tenth day, and on the following day he died.

Case 7.—Patient No. 86: A female, age 45, was admitted to the Royal Victoria

Hospital following severe burns to the chest and abdomen. The wounds were cleansed and tannic acid was applied. She was not seen until the sixth day, when a blood specimen was obtained. No histamine was found in the blood and the patient died on the following day. There was no autopsy.

Discussion.—From a survey of the results obtained in the present studies, it will be observed that following severe burns, changes in the blood histamine level occur which may be divided into three distinct phases. First, a marked increase in the blood histamine which is present within an hour occurs in certain cases. Later, in all cases, a rapid and marked decrease takes place, the blood histamine content reaching its lowest level on the third to fifth day, the time at which edema and the signs of toxemia are most marked. There appears to be some correlation between the degree of damage and edema, and the decrease in the blood histamine, for such a decrease is most marked in the severe cases, and from Chart 4, it will be seen that in each instance where death occurred, the histamine content of the blood was well below the normal level 16 to 24 hours previously. As the edema subsides, the histamine level of the blood returns to normal or above. Such an increased blood histamine level may persist for some time. Of these three phases, that most consistently observed is the marked decrease in the histamine content of the blood as edema develops.

Previous investigations on blood histamine content in cases of burns by Barsoum and Gaddum,[12] and Code and MacDonald[15] showed an increase in the blood histamine after the fourth or fifth day. The present investigations indicate that while an increase may occur at this time (as in Case 1 of our series) the blood histamine does not always rise above the normal. Barsoum and Gaddum[12] interpreted this rise as a possible cause of burn shock, whereas the present studies show that it occurs as the clinical condition of the patient is improving. It is probably for this reason that they had difficulty in attempting to correlate these changes with the onset of shock. Further examination of their results reveals that the blood histamine level was beginning to decrease in the cases that died. Although their diagrams do not indicate the actual day on which the determinations were made, a decrease in the blood histamine was apparently occurring in Case 1, and no determinations were made in Case 4 for at least four days before death. There was, however, a beginning decrease in the blood histamine level at this time. Thus, both in burns and in shock due to trauma or surgical intervention, a marked decrease in the histamine content of the blood occurs (Rose and Browne[16]). This is, therefore, contrary to the original conception that the histamine content of the blood must be increased during shock.

These results may perhaps be explained on the basis of previous work. In studies on allergic patients, one of us (Rose[20]) has shown that stimulation of the skin of a patient with dermatographia may lead to rapid increase in the blood histamine which, in turn, is followed within 20 minutes by a decrease to below the original level as wheal formation takes place. Thus, as postulated by Lewis,[21] irritation of the skin may result in a release of histamine. It has

been noted, further, that following the production of a large area of edema, such as is occasionally seen after the subcutaneous injection of a vaccine, or during the stage of swelling in angioneurotic edema, a marked reduction of the blood histamine usually occurs (Rose[20, 22]).

At this point, it may be well to note that in certain blood dyscrasias the total blood histamine may be increased as much as one hundred times without any symptoms being produced referable to the histamine (Code and MacDonald,[15] Rose[23]). This is due to the fact that under these circumstances the greatest portion of the blood histamine is held within the cellular elements (Code[24]), and, as such, it is inactive. It is only when histamine is released from the cells of the blood into the plasma that it becomes active. On the other hand, a decrease in the blood histamine has been observed only during shock, or when marked edema of the skin and superficial tissues is present (Rose[16, 20, 22]). Since a decrease in the blood histamine to below normal levels is usually correlated with such symptoms, it is felt that it may be of more clinical significance than an increase. This argument is supported, further, by the observation that following the subcutaneous injection of histamine, there is a decrease in the blood histamine as symptoms are produced (Rose[25]), and this has also been noted following the intravenous administration of histamine (Rose[26]).

In connection with the secondary increase of histamine in the blood, which is seen after the fourth or fifth day, it is interesting to note that an increase in the blood histamine has been observed in cases of chronic irritation of the skin (Rose[22]).

Loos[27] has expressed the opinion that that histamine may increase in the tissue about an area of inflammation, and this has actually been demonstrated in rabbits by Rocha E Silva and Bier,[28] and Tarras-Wahlberg.[29] Following the production of burns in dogs, Kisima[30] observed an initial increase in the histamine content of the blood followed in two to three days by a decrease. These changes were accompanied by an increase in the histamine content of the spleen, liver and pancreas. It may be that histamine is concerned with the shift of fluid from intra- to extracellular spaces and is, itself, transferred to the area of edema, whether it be the skin and superficial tissues, or the viscera.

The value of blood studies as a guide to the treatment of shock has been emphasized by Moon[31] and Scudder.[19] Although it is agreed that hemoconcentration is a criterion of shock, we have been struck by the number of instances where it was not present although, clinically, the patient was in shock, with a falling blood pressure and an increasing pulse rate. In all such cases, as, indeed, in others when hemoconcentration is manifest, the histamine content of the blood is always decreased to below normal. In the present studies, Case 3 illustrates a type of death which may have been influenced by the initial hemoconcentration. Yet, on the day of death, blood studies were normal with the exception of the blood histamine which was markedly decreased. In previous studies (Rose and Browne[16] and Rose, Weill and

Browne[32]) it has also been noted that patients may die in spite of the intravenous administration of amounts of plasma adequate to overcome hemoconcentration, as controlled by blood studies. The hemoglobin, hematocrit, plasma protein and other constituents of the blood, such as the chlorides, sodium and potassium may not be significantly altered under these conditions, but in all instances, there is marked diminution of the histamine content of the blood. As shown in the present cases, the administration of plasma may markedly reduce hemoconcentration without affecting the course of the blood histamine. A possible explanation is that the histamine remains low as long as the tendency to loss of fluid from the blood stream continues, even though by the use of intravenous fluids the blood volume may have been restored to normal so that no actual hemoconcentration exists at the time of taking the specimen. Thus, the blood histamine might be regarded as reflecting some process more fundamental than hemoconcentration in the causal chain of events leading to shock. From the present evidence, one cannot determine whether the changes in blood histamine are in any way causally related to the mechanism of hemoconcentration and shock. A reconsideration of its possible importance seems however to be justified since histamine shock, and shock due to trauma or burns may all be correlated with a decrease in the histamine content of the blood.

CONCLUSIONS

(1) Studies on the blood histamine, hemoglobin, hematocrit and plasma proteins have been made in seven patients following severe burns.

(2) It has been shown that a marked increase in the blood histamine occurs in certain cases within one hour after the burn. In all cases, there is a decrease in the blood histamine as toxemia and edema appear. As the edema and signs of toxemia disappear with the clinical improvement of the patient, the blood histamine rises to normal or higher levels. Such secondary increases in the blood histamine may persist above the normal for some time.

(3) There appears to be a definite correlation between the degree of damage and the decrease in the histamine content of the blood. Thus, the most marked decrease in the blood histamine has been noted 12 to 36 hours before death. Similar findings have been observed in other cases of fatal shock.

(4) Changes in the blood histamine do not appear to be altered by the administration of plasma in amounts sufficient to control hemoconcentration.

(5) These findings are discussed in relation to the changes observed in the histamine content of the blood in other conditions.

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A STUDY OF THE WEIGHT OF THE CELIAC GANGLION AND ITS RELATIONSHIP TO ESSENTIAL HYPERTENSION

REPORT UPON 201 CELIAC GANGLIA

MEYER O. CANTOR, M.S., M.D.

DETROIT, MICH.

FROM THE DEPARTMENT OF PATHOLOGY, WAYNE UNIVERSITY, COLLEGE OF MEDICINE, DETROIT, MICH.

THE TREATMENT OF ESSENTIAL HYPERTENSION, which for so many years had been purely a medical problem, is now being taken up by surgeons all over the world. The surgical attack upon the problem of essential hypertension is quite varied. The exact surgical procedure employed is dependent upon the etiologic concept held by the surgical center where the patient happens to be. There are three surgical concepts of the etiology of essential hypertension, and as a result there are three methods of operative attack.

The first surgical concept considers essential hypertension as being due to hyperepinephrinemia. This theory is supported by De Courcy.[8] The literature refuting this concept is voluminous.[2, 9, 11, 15, 17, 18, 19]

The second surgical concept is the neurogenic theory held by Max Peet[10] and the Mayo Clinic.[1] This concept, also, has been vigorously attacked by many recent workers, particularly by Goldblatt and his coworkers.[12, 13, 14]

The third theory with surgical potentialities is that of Crile.[4–7] This theory states that "only those individuals who have by inheritance large celiac and aortic ganglia can and do have hypertension."[4, 5] Crile[4] states that the average weight of the ganglion in cases of essential hypertension is 1,015 mg. for the left ganglion, and 669 mg. for the right ganglion. In the nonhypertensive group that he reported, the average weight of the celiac ganglion was found to be 310 mg. for the left ganglion, and 350 mg. for the right ganglion in cases of epilepsy. In recurrent hyperthyroidism, he found the average weight of the left celiac ganglion to be 235 mg., and the average weight of the right celiac ganglion to be 271 mg. In a group of cases with neurocirculatory asthenia, Crile reported the average left ganglionic weight as being 205 mg., and the right ganglionic weight 340 mg. In recent papers,[6, 7] Crile states that the normal weight of the celiac ganglion in the nonhypertensive individual varies from 250 to 350 mg. The photographs shown by him also tend to show the markedly greater size of the celiac ganglion in cases of hypertension as compared with the celiac ganglion in nonhypertensive individuals.

The present study was undertaken for the purpose of determining the weight of the normal celiac ganglion and for the further purpose of testing the relationship of the size of the ganglion and essential hypertension. The literature does not contain such data as is presented here.

Anatomy of Celiac Ganglion.—The anatomic descriptions given for the celiac ganglia differs with almost every author. The celiac ganglion has been described as being as large as a "nickel,"[4] or a "strawberry."[16] One anatomic

text describes it as being one inch in diameter.[3] Many authors speak of its semilunar shape,[20] although most writers note variability in regard to this. Crile noted that the left celiac ganglion was usually larger than the right and he was the first to report the weight of the ganglia. All writers have uniformly agreed that the greater splanchnic nerve joins the celiac ganglion at the upper outer pole of the ganglionic mass.

In the series of cases which we studied (201 ganglia), we found a great variation in the size, shape, and weight of celiac ganglia. The left celiac ganglion was usually found to be larger than the right; the difference in size being very marked in some cases—in which the left ganglion was two to three times the size of the right. However, in many cases the weight of the right and left ganglia were almost equal. Occasionally, the right ganglion was found to be larger than the left. This difference in size has been unexplained as yet. It is possible that it may have to do with the close approximation of the left celiac ganglion to the aorta. A second possibility has to do with the possible relationship between the human "left brainedness" and the larger left celiac ganglion. Functionally, however, since the area of nervous distribution is greater from the right than from the left celiac ganglion, one might expect the right ganglion to be the larger. Such was not usually found to be the case.

It was usually very difficult to separate the left ganglion from the adventitia of the aorta. Often, in the process of separation, the adventitia of the aorta was found attached to the under surface of the left ganglion. The right ganglion could easily be dissected free and the right aorticorenal ganglion could usually be differentiated from the celiac ganglion, whereas, on the left side, the aorticorenal ganglion was often fused with the left celiac ganglion to form a single fleshy mass.

Uniformly, the left celiac ganglion rested directly upon the aorta, whereas the right celiac ganglion rested upon the right crus of the diaphragm, under the inferior vena cava. In the vast majority of the ganglia that we dissected, the greater splanchnic nerve did not join the celiac ganglion at the upper outer pole of the ganglion, but rather joined it at its postero-inferolateral pole. We used this point of union with the greater splanchnic nerve to determine the lower limit of the celiac ganglion. The fleshy mass below this was considered as being aorticorenal. As stated, on the left side the aorticorenal ganglion is so intimately blended with the celiac ganglion that it was often impossible to separate them. Using our arbitrary lower limit of celiac ganglion as the point of junction of the greater splanchnic nerve with the ganglion, we cut the ganglionic mass flush with this point of union of the greater splanchnic nerve and the celiac ganglion. As a result, our specimens should represent celiac ganglion alone. For purposes of orientation on the specimens, the terminal half centimeter of greater splanchnic nerve was left attached to the celiac ganglion. On the right side, the aorticorenal ganglion was usually joined to the celiac ganglion by nerve fibers which were cut with ease. On this side, the lesser splenchnic nerve joins the lower ganglionic mass (aorticorenal ganglion) and the greater splanchnic nerve joins the upper ganglionic mass (celiac ganglion).

At times, both splanchnic nerves pierce the crus of the diaphragm at the same point, and travel together to the point of union of the greater with the celiac ganglion. Just before this union is made, the lesser splanchnic nerve may be seen coming off from the conjoined trunk and passing downward to the aorticorenal ganglion to unite with it. At times the greater and lesser splanchnic nerves do not travel together but pierce the crus of the diaphragm through separate openings. Invariably the greater splanchnic nerve pierces the diaphragmatic crus above the lesser splanchnic; the latter then comes out below and medial to the point of emergence of the greater splanchnic nerve. The same relationship of the two splanchnic nerves exists on the left side, but here the aorticorenal ganglion is so intimately blended to the celiac ganglion that the whole constitutes one large fleshy mass.

Usually the greater splanchnic nerves, after running along the vertebral column in a longitudinal course pierce the crura of the diaphragm on each side, and then suddenly make a right-angle turn medially and terminate in the celiac ganglion of the particular side at the postero-inferolateral angle of the ganglion. Often the greater splanchnic nerve passes behind the upper end of the celiac ganglion and gives one the impression that it is joining the upper end of the ganglion, but actually it passes downward behind the ganglion to join the ganglion at its lower outer pole; this anatomic feature provides a satisfactory boundary for determining the lower limit of the celiac ganglion. Sometimes the right-angle turn made by the greater splanchnic nerve forms a loop with a diameter of one centimeter. In almost all cases one can easily pick up the greater splanchnic nerve by passing the index finger downward along the bodies of the lumbar vertebrae and the crura of the diaphragm. When the palpating finger reaches the greater splanchnic nerve at its right-angle turn, the finger is halted by the loop formed by the angular turn of the nerve as it approaches the ganglion. Occasionally, the greater splanchnic nerve emerges from behind the crus of the diaphragm at a point one to two centimeters higher up than the celiac ganglion. In such cases, it passes downward in a straight course lying upon the crus of the diaphragm and then makes a right-angle turn medially and forward when it reaches the level of the celiac ganglion. The greater splanchnic nerve, in its abdominal course, varies from 0.2 to 0.4 cm. in thickness and is quite resistant to tearing.

There is an extreme degree of variation in the size of celiac ganglia. Some ganglia are one-half centimeter from side-to-side, and others measure two to three centimeters in the same dimension. The greatest diameter was generally from the lateral to the medial edge of the ganglionic mass, although in some of the triangular ganglionic masses the vertical measurements was the largest. There was also some degree of variation in thickness, but not to the same degree as in the other measurements. Some of the ganglia were about 0.2 cm. thick, while others measured almost 0.7 cm in thickness. Figures 1–4 show some of the variations in size and shape found in celiac ganglia.

Variations in Ganglionic Weight with Sex, Age, and Size of Individual.—There was an extreme degree of variation in weight of the ganglia which

ranged from small ones weighing 270 mg. to very large ones weighing 2,000 mg. Among adults there was no correlation between the size of the individual and the size of the celiac ganglion. Some of the largest individuals had the smallest ganglia and *vice versa*. In three cases of pituitary dyscrasia in women who were found to weigh well over 300 pounds and to be over six feet tall, the celiac ganglia were found to be among the smallest in our collection.

FIG. 1. FIG. 2.

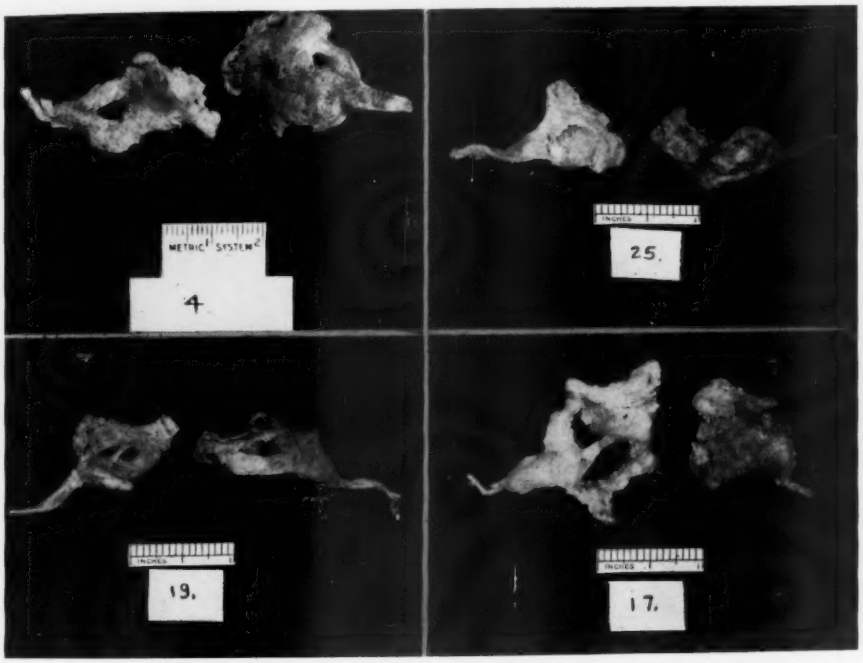

FIG. 3. FIG. 4.

FIG. 1.—Left ganglion 1,466 mg. Right ganglion 1,082 mg. Patient: L. W., age 50, B.P. 138/84. Diagnosis: Gangrene of leg.
FIG. 2.—Left ganglion 1,284 mg. Right ganglion 1,037 mg. Patient: H. L., age 67, B.P. 130/70. Diagnosis: Pneumonia.
FIG. 3.—Left ganglion 1,330 mg. Right ganglion 1,113 mg. Patient: A. P., age 50, B.P. 120/80. Diagnosis: Pneumococcus meningitis.
FIG. 4.—Left ganglion 1,984 mg. Right ganglion 1,968 mg. Patient: L. G., age 55, B.P. 120/80.

Age appeared to be quite important in determining the size of the celiac ganglia. An examination of Charts 1 and 2 readily shows that there is an increase in weight of the celiac ganglia from birth to the 40- to 55-year-old group. After the age of 55, there tends to be a progressive decrease in the weight of the celiac ganglia. In the newborn, term infant, the average weight of the left celiac ganglion varies from 75 to 150 mg., and the right celiac ganglion weighs 50 mg. From infancy to the age of puberty, a progressive but not remarkable increase in the weight of the celiac ganglia can be noted (see tabulated case records). At the age of puberty, there appears to be a remarkable increase in the size of the celiac ganglia from the childhood to adult levels of weight. The ganglia in the 20- to 30-year-old group ranged from 400

to 900 mg. Only one ganglion in this age-group weighed as much as 1,400 mg. In the 30- to 40-year-old group, the general average of the weight of the ganglia was found to be about the same as in the previous age-group. The general average for this group was 814 mg. for the left ganglion, and 723 mg. for the right ganglion. The 40- to 50-year-old group had the largest-sized celiac

FIG. 5.

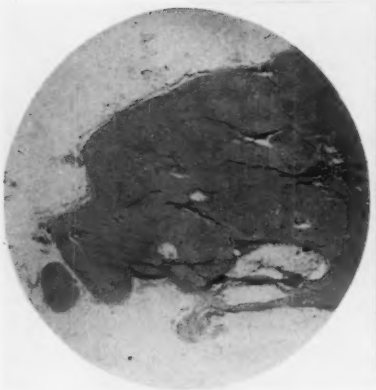

FIG. 6.

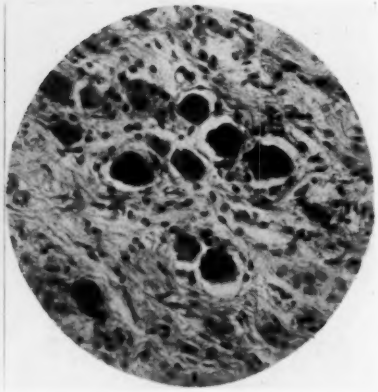

FIG. 7.

FIG. 5.—Photomicrograph of small celiac ganglion. (×20) Note the small amount of extraneous tissue about the ganglion.

FIG. 6.—Photomicrograph of large celiac ganglion. (×15) Note the small amount of extraneous tissue about the ganglion.

FIG. 7.—Photomicrograph of celiac ganglion showing characteristic histologic appearance of human celiac ganglion, *i.e.*, groups of ganglion cells with dendritic fascicular tracts. (high power)

ganglia. In this group, the large-sized ganglia, not infrequently, weighed over 2,000 mg. It would seem that the celiac ganglia reach their maximum size during this decade. Following the 65-year-old group there appears to be a definite decline in the weight of the celiac ganglia. One of the smallest ganglia in our series was removed from a patient age 81.

The sex of the patient appears to account for a demonstrable weight difference. The average weight of the male celiac ganglion is greater than that of the female. The average weight of the left celiac ganglion in males was

found to be 1,140.5 mg., and the average weight of the left celiac ganglion in females was 779 mg. The average weight of the right celiac ganglion in the male was 894.3 mg., and that of the right celiac ganglion in females was 561 mg. The largest celiac ganglion in our series was found in a man. It weighed 2,100 mg. The largest celiac ganglion removed from a woman weighed 1,461 mg.

Relationship between the Weight of the Celiac Ganglia and Essential Hypertension.—One of the foremost exponents of the surgical treatment of essen-

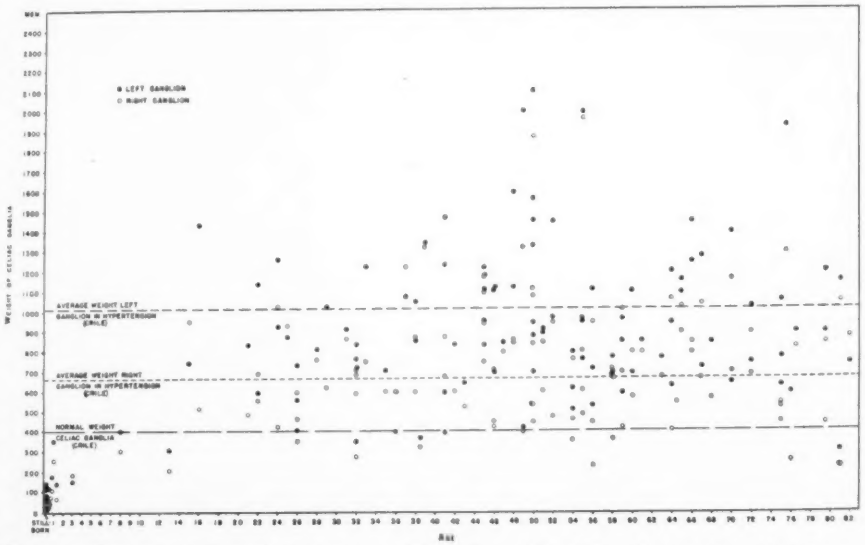

CHART 1.—Diagnosis: Pneumonia. Scattergram plotting the weight of the celiac ganglia against the age of the patient.

tial hypertension (Crile) bases his etiologic concept upon the premise that, "the celiac ganglion is larger in the individual with essential hypertension than in the nonhypertensive." He quotes the weight of the left ganglion as being 1,015 mg. in hypertensive individuals, and that of the right as being 669 mg., whereas the average normal ganglionic weight was only 350 mg. If it is true that the celiac ganglia are larger in individuals with essential hypertension than they are in nonhypertensives, then the operation of celiac ganglionectomy, based upon the above premise, is justifiable. If it is not true then the whole hypothesis has no basis since its premise is false.

Method.—With the idea of substantiating Crile's statements as to the weight of the celiac ganglion, we collected a large number of celiac ganglia. Our ganglia were all removed from autopsy material as soon after death as possible. The celiac ganglia were identified by following the greater splanchnic nerve at its point of emergence from behind the crus of the diaphragm. The terminal centimeter of the greater splanchnic nerve was removed with the celiac ganglion for purposes of identification, as can be readily noted in Figures 1–4. The ganglia were cut flush with the point of attachment of the greater splanchnic nerve, as we considered everything below

this point to be aorticorenal ganglion. After the removal of the ganglia, they were thoroughly dissected free of all extraneous material, and were then weighed on a fine balance inclosed in a glass case, and the weighing was carried to the milligram. Several ganglia were serially sectioned and microscopically examined to note the amount of extraneous tissue present. Figures 5 and 6 show the very small amount of extraneous tissue present after the dissection. After the ganglia had been removed, some of the earlier ones had been put into a bottle of 10 per cent formalin and suitably labelled as to right

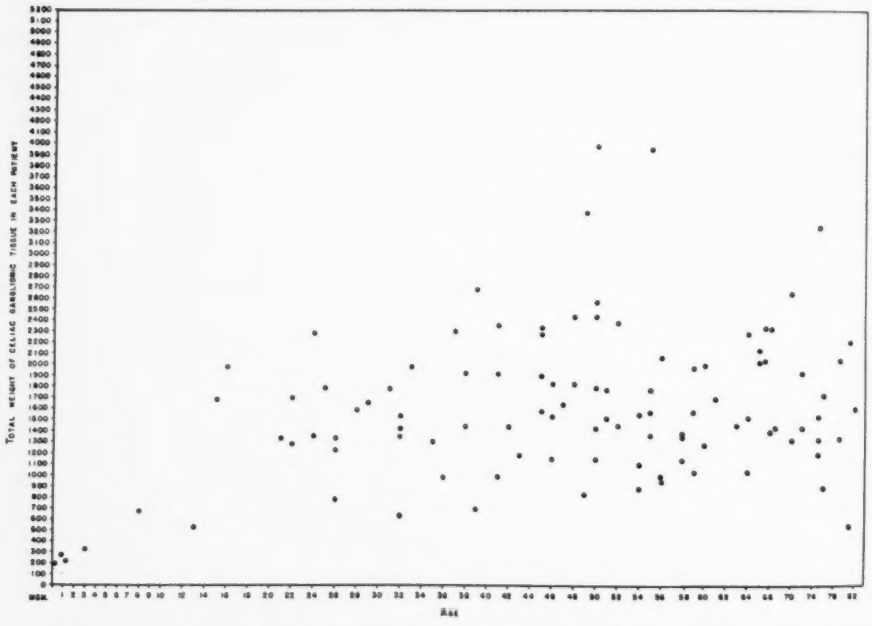

CHART 2.—Scattergram plotting the total ganglionic weight obtained by adding the weights of the left and right celiac ganglia against the age of the patient. The total ganglionic weight reported in his hypertensive group was 1,682 mg. (Crile.)

or left side. These ganglia were not dissected clean or weighed for five weeks. In order to determine whether the fixation in formalin would add materially to the ganglionic weight, three of the ganglia were weighed in the fresh state immediately after removal and dissection, and were then weighed at varying intervals of time subsequently. By so doing, we found that the celiac ganglia increased in weight for the first week. During this period of time between 15–20 mg. of weight was added to the original weight of the fresh ganglion. After the first week, however, there was a progressive loss of weight, such that by the end of the fifth week the celiac ganglia weighed from 25–40 mg. less than they did in the fresh state.

It is thus apparent that the celiac ganglia do not gain weight when immersed in formalin after the first week. Since the ganglia in our series were either weighed immediately after the autopsy or five weeks later, it is apparent that we are being conservative in determining the true celiac ganglionic weight since we did not add the known loss of weight to the resulting weight obtained

at the end of five weeks' fixation. The celiac ganglionic weights obtained in our series of ganglia were all uniformly higher than those obtained at the Cleveland Clinic. The small tag of greater splanchnic nerve which we permitted to remain attached to the celiac ganglia does not add materially to the final result, and, certainly, does not account for the wide difference between our results and those of the Cleveland Clinic.

Results.—An attempt was then made to correlate the size of the celiac ganglia with the blood pressure of the patient in order to determine whether

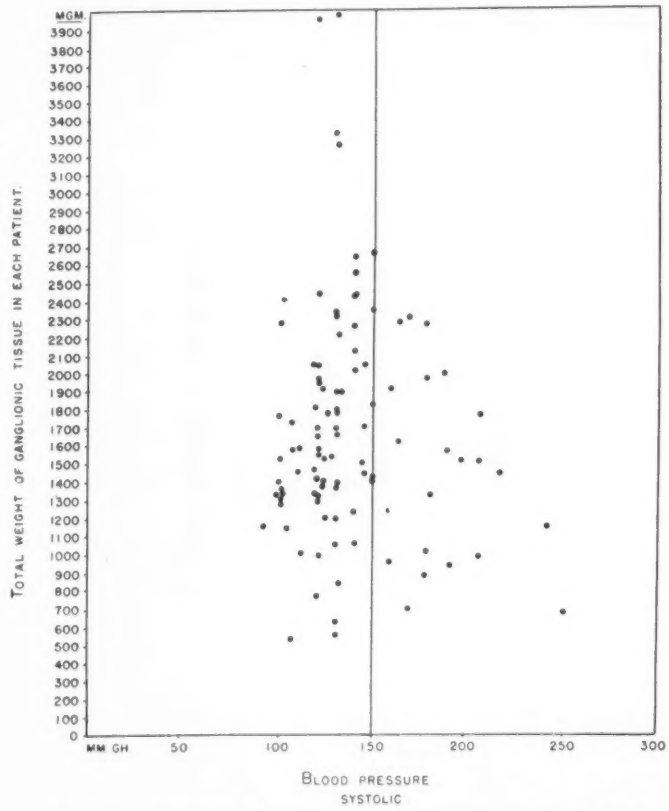

CHART 3.—Scattergram plotting the total ganglionic weight against the systolic blood pressure. Note that the total ganglionic weight reported in Crile's hypertensive group was 1,682 mg.

there was really an increase in size of the celiac ganglia in hypertensive individuals. An examination of Charts 1, 2, and 3 furnishes adequate evidence that the vast majority of the large ganglia weighing in the neighborhood of 1,000 mg., or more, were well within the normal blood pressure range, and that in the hypertensive group the celiac ganglionic weights were actually somewhat less than in the nonhypertensive group. The largest ganglion collected weighed 2,100 mg., and was found in a nonhypertensive individual, whereas the largest ganglion found in an hypertensive individual weighed 1,250 mg. Both these ganglia were on the left side. The right celiac ganglion

that was the largest in the nonhypertensive group weighed 1,950 mg., while the heaviest right celiac ganglion in the hypertensive group weighed 1,225 mg. On Figure 5 a cross-line, indicating the level which the Cleveland Clinic considers to be the normal celiac ganglionic weight in the nonhypertensive group (350 to 400 mg.), is seen to be far below the average weight of the celiac ganglia in our nonhypertensive group. Practically all of the celiac ganglionic weights in the nonhypertensive group in our series of 200 ganglia fall well within the range of ganglionic weights quoted by Crile as character-

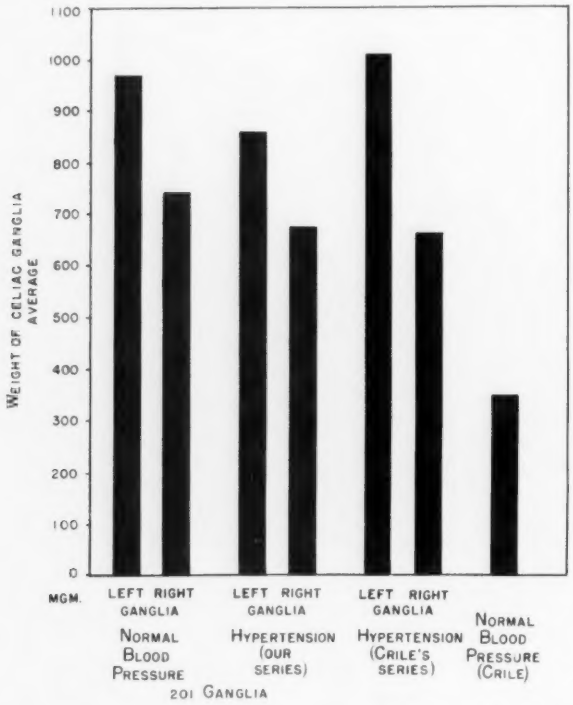

CHART 4.—Graphic presentation of the average weight of the left and the right celiac ganglia in our series of hypertensive and nonhypertensive individuals as compared with Crile's results for the same groups.

izing the hypertensive group. Chart 4 is a graphic representation of the average weight of the left and right celiac ganglia in our series of cases in the nonhypertensive group and in the hypertensive group, in comparison with the statistics quoted by Crile for the same two groups in his series. A survey of this shows that the average weight of the left celiac ganglion in our nonhypertensive group was 968.4 mg., and the average weight of the right celiac ganglion in our nonhypertensive group was 745 mg. The average weight of the left celiac ganglion in our hypertensive group was seen to be 867.9 mg., and the average weight of the right celiac ganglion in the hypertensive group was found to be 674.4 mg.

These results, when considered in the light of the difference in the numbers of cases in each group, reveals a startling uniformity of result. It becomes

quite obvious that the hypertensive group do not have larger celiac ganglia than the average normal nonhypertensive in the same age-group, and also that the average normal ganglionic weight is far greater than that quoted by Crile. The amazing equality of ganglionic weights in our group of normal individuals, and in Crile's group of hypertensive individuals can mean only one thing—that is, that there is no difference in the celiac ganglionic weight in the nonhypertensive and in the hypertensive individual, and that our equality in the average weights obtained in both groups merely represents the mean average of the celiac ganglionic weights on the left and right side in all individuals, irrespective of the presence or absence of hypertension.

SUMMARY AND CONCLUSIONS

(1) The greater splanchnic nerve unites with the celiac ganglion at the postero-infero-external angle (of the ganglion) and not at the upper pole as formerly stated.

(2) The celiac ganglia vary greatly in size and shape. No two ganglia have exactly the same shape. The point of union of the greater splanchnic nerve with the lower pole of the celiac ganglion, we considered as being the lower limits of the celiac ganglion proper, everything below this point, we called the aorticorenal ganglion.

(3) The celiac ganglia increase in size from birth until the age of 40 to 55 years. In this age-group, the celiac ganglion appears to attain its maximum size and weight. After this is a gradual decline of the ganglionic weight to a level that, in the octogenarians, is near the childhood level.

(4) The left celiac ganglion is uniformly larger than the right.

(5) There is a definite difference in the sizes of the celiac ganglia in the two sexes. The largest ganglia were found in the male sex.

(6) There is no correlation between the weight of the celiac ganglion and essential hypertension. The average weight of the celiac ganglion in the hypertensive group was somewhat less than the average weight of the ganglia in the nonhypertensive group. This was undoubtedly due to the difference in the number of cases in each group.

(7) Our average weight of the left celiac ganglion in the nonhypertensive group was 969 mg. This coincides closely with the average weight of the left celiac ganglia removed by Crile surgically from hypertensives (1,015 mg.).

(8) The average weight of our right celiac ganglia in the nonhypertensive group was 745 mg. This was somewhat higher than the weight of the right celiac ganglion reported by Crile for his hypertensive group (667 mg.).

(9) The total ganglionic weight in Crile's hypertensive group was 1,682 mg., whereas the total ganglionic weight in our nonhypertensive group was 1,714 mg. The total ganglionic weight represents the sum of the weights of the left and the right celiac ganglia in each individual.

(10) From the preceding data, we feel that new standards of weight for the celiac ganglia should be established; and that there is no relationship between the weight of the celiac ganglion and essential hypertension.

TABLE I

SUMMARY OF DATA RELEVANT TO CELIAC GANGLIA EXAMINED IN 101 CADAVERS

	Name	Age in Years	Left in Mg.	Right in Mg.	Sex	Blood Pressure	Diagnosis
1.	B. M.	8	400	281	M.	250/158	Polycystic kidneys
2.	M. H.	13	313	207	F.	115/75	Diabetic coma
3.	J. L.	15	745	943	F.	144/80	Rheumatic pancarditis
4.	L. G.	16	1,461	514	F.	120/80	Miliary tuberculosis
5.	E. O.	21	834	485	F.	120/80	Tuberculous peritonitis
6.	J. C.	22	581	691	F.	100/60	Bacterial endocarditis
7.	S. S.	22	1,135	564	M.	120/80	Peritonitis
8.	M. H.	24	928	428	F.	126/78	Intestinal obstruction
9.	W. K.	24	1,252	1,021	M.	180/120	Chronic nephritis, with uremia
10.	W. C.	25	865	929	M.	132/88	Tuberculous meningitis
11.	W. F.	26	730	600	F.	100/70	Peritonitis
12.	J. F.	29	1,026	628	F.	130/80	Postpartum hemorrhage
13.	M. L.	26	405	358	F.	120/80	Acute pancreatitis
14.	H. P.	31	913	864	F.	128/80	Puerperal sepsis
15.	G. L.	28	816	767	F.	110/70	Septicemia
16.	J. R.	26	568	465	F.	140/95	Degeneration of liver
17.	R. R.	32	722	682	M.	120/80	Mesenteric thrombosis
18.	W. D.	32	832	704	M.	100/60	Lung abscess
19.	E. G.	32	765	594	F.	102/60	Peritonitis
20.	M. R.	32	353	270	F.	130/80	Pneumonia
21.	S. R.	33	1,226	748	F.	120/75	Subphrenic abscess
22.	P. L.	35	702	596	F.	101/78	Carcinoma of breast
23.	E. F.	36	395	590	F.	120/80	Lobar pneumonia
24.	L. L.	37	1,073	1,224	M.	165/110	Intestinal obstruction
25.	S. M.	38	852	605	F.	110/70	Angiosarcoma
26.	L. D.	38	1,047	871	M.	128/80	Brain abscess
27.	F. J.	39	1,340	1,333	M.	150/90	Brain tumor
28.	F. L.	39	371	325	F.	170/130	Brain tumor
29.	G. D.	41	1,236	675	F.	134/80	Peritonitis
30.	N. Q.	41	600	392	F.	110/60	Bacterial endocarditis
31.	T. B.	41	1,471	882	M.	150/70	C.N.S. syphilis
32.	L. E.	42	837	605	F.	220/100	Chronic nephritis, with uremia
33.	H. B.	45	955	945	M.	130/80	Bacterial endocarditis
34.	S. S.	43	653	532	F.	125/80	Carcinoma uterus
35.	C. P.	45	826	747	M.	120/80	Myocarditis
36.	M. B.	45	1,216	1,101	M.	170/90	Cerebral hemorrhage
37.	Z. L.	45	1,102	1,170	M.	100/68	Pneumonia
38.	A. K.	46	1,120	420	M.	129/86	Perinephritic abscess
39.	M. D.	46	1,112	701	F.	150/70	Acute thyroid crisis
40.	A. F.	46	700	450	F.	90/65	Bacterial endocarditis
41.	W. S.	47	857	792	M.	120/80	Cirrhosis of liver
42.	O. G.	48	1,594	836	M.	140/70	Pyonephritis
43.	P. M.	49	2,005	1,316	M.	130/80	Peritonitis
44.	P. C.	49	432	405	F.	134/82	Carcinoma of cervix
45.	C. W.	50	696	457	M.	240/130	Nephrosclerosis, with uremia
46.	F. F.	50	2,100	1,870	M.	130/80	Pneumonia
47.	J. P.	48	1,121	680	M.	120/80	Bacterial endocarditis
48.	L. L.	50	1,570	—	M.	125/80	Pneumonia
49.	M. B.	50	956	844	M.	130/80	Leukemia
50.	L. W.	50	1,466	1,082	M.	138/84	Gangrene of leg
51.	A. P.	50	1,330	1,113	F.	120/80	Pneumococcus meningitis
52.	E. E.	51	894	613	M.	200/120	Pontine hemorrhage
53.	A. B.	51	906	860	M.	100/60	Lung abscess
54.	T. B.	52	1,441	944	F.	104/88	Cardiac failure; rheumatic heart disease
55.	R. L.	52	973	475	M.	145/90	Leukemia
56.	H. M.	50	887	534	F.	150/84	Carcinoma of cervix
57.	B. R.	54	514	362	F.	180/100	Carcinoma of liver
58.	G. W.	54	622	470	F.	130/80	Acute pancreatitis
59.	E. H.	54	790	765	F.	120/84	Carcinoma of sigmoid
60.	L. G.	55	1,984	1,968	M.	120/80	Lobar penumonia
61.	E. Z.	55	965	612	F.	110/70	Lobar pneumonia
62.	M. G.	55	961	808	F.	210/100	Ovarian hemorrhage

TABLE I (*Continued*)

	Name	Age in Years	Left in Mg.	Right in Mg.	Sex	Blood Pressure	Diagnosis
63.	E. C.	55	768	590	M.	128/80	Bronchogenic carcinoma
64.	G. H.	56	715	235	F.	160/110	Pulmonary embolus
65.	R. S.	56	1,115	944	F.	122/78	Pneumonia
66.	C. A.	58	763	380	F.	105/70	Myelogenous leukemia
67.	L. K.	56	531	432	F.	210/115	Cerebral hemorrhage
68.	E. P.	58	687	693	F.	120/80	Pneumonia
69.	H. C.	58	706	678	F.	125/80	Postoperative peritonitis
70.	P. H.	59	963	1,008	M.	180/120	Coronary occlusion
71.	L. B.	59	868	701	F.	190/110	Peritonitis
72.	A. M.	59	596	435	F.	180/140	Nephrosclerosis, with uremia
73.	M. V.	60	713	576	F.	120/70	Carcinoma of stomach
74.	H. C.	60	1,135	865	M.	190/120	Coronary occlusion
75.	A. Y.	61	865	832	M.	130/80	Lobar pneumonia
76.	F. G.	63	777	677	M.	118/84	Tuberculous kidney
77.	G. P.	64	1,200	1,065	M.	140/88	Carcinoma of bladder
78.	D. G.	64	950	560	F.	125/75	Carcinoma of ovary
79.	M. Z.	64	633	408	M.	140/90	Cerebral hemorrhage
80.	A. H.	65	1,090	917	M.	140/80	Cardiac failure; aortic stenosis
81.	A. A.	65	1,124	1,005	M.	140/90	Chronic nephritis
82.	S. S.	66	1,245	796	F.	148/82	Myocardial failure; arteriosclerotic heart disease
83.	J. B.	66	1,467	854	M.	130/90	Aortic stenosis
84.	H. I.	67	1,284	1,037	M.	130/70	Pneumonia
85.	A. P.	67	724	672	F.	104/60	Carcinoma of pancreas
86.	S. L.	68	856	569	M.	145/86	Pyonephritis
87.	A. S.	70	638	679	M.	120/70	Lobar pneumonia
88.	J. C.	70	1,485	1,161	M.	140/80	Carcinoma of prostate
89.	L. C.	72	745	681	F.	150/80	Cardiac failure; arteriosclerotic heart disease
90.	J. T.	72	1,028	897	M.	160/104	Coronary occlusion
91.	K. S.	75	635	558	F.	130/84	Pneumonia
92.	R. F.	75	1,052	453	F.	210/120	Cardiac failure; essential hypertension
93.	A. F.	75	783	527	F.	180/100	Carcinomatosis
94.	M. F.	75	1,921	1,324	M.	130/80	Coronary occlusion
95.	A. P.	76	663	267	F.	192/110	Cardiac failure; essential hypertension
96.	M. S.	76	897	828	M.	110/70	Carcinoma of liver
97.	J. R.	79	1,195	851	M.	118/80	Carcinoma of pancreas
98.	H. H.	79	894	445	M.	100/60	Abscess of kidney
99.	S. W.	81	317	234	F.	130/80	Ovarian hemorrhage
100.	R. B.	81	1,152	1,052	M.	136-78	Cystic liver
101.	L. T.	82	763	876	M.	165/90	Cardiac failure; arteriosclerotic heart disease

The author wishes to express his appreciation to Dean Edgar Norris for his many helpful suggestions and guidance during the course of this study.

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MALIGNANT TUMORS OF SYNOVIAL ORIGIN

CRENSHAW D. BRIGGS, M.D.

WASHINGTON, D. C.

DURING the last decade, and particularly the last three years, a small group of investigators has endeavored to add to our very limited knowledge of malignant tumors which take their origin from the synovial-lined structures, namely, joints, bursae and tendon sheaths. This field has too long remained neglected by pathologists. Owing both to the relative infrequency of these tumors and, what is more likely, the failure to classify them properly, the number of cases reported has been small. It has been difficult, therefore, to draw any conclusions as to the most satisfactory method of treating them. This report is based on the cases on file at the Army Medical Museum upon which the diagnosis of synovioma has been made. Its purposes are to increase the present small number of previously reported synoviomata, to point out the microscopic pathology characteristic of the majority of these cases, and to suggest a plan of treatment which, in the light of our limited knowledge, seems both rational and conservative. Where the material has been received from physicians in civilian practice, it has been impossible in some instances to obtain an adequate description of the gross pathology as well as a complete history and follow-up.

This study treats only with those tumors arising from the joint capsule, bursal wall or tendon sheath which are malignant, or border-line, and does not include the more common giant cell tumor or xanthoma which may arise from either of the three structures. The term synovioma was first coined by Lawrence Smith[1] to designate those tumors arising from all three synovial-lined structures. This marked a departure from the old method of classifying these new growths separately. The earlier reports were further clouded by the confusion surrounding the actual origin of synovial tissue. For a long time it was held to be endothelial in character and, on this basis, tumors arising from these structures were designated as endothelial sarcoma, angiosarcoma, and endothelioma. The synovial membrane is now generally accepted as mesenchymal in origin. It may be divided into two parts histologically—the outer wall, which is composed of dense connective tissue known as the fibrous layer, and the inner or synovial layer, which is more cellular and thought by many to secrete the viscid colorless liquid of the joint cavity. The transition between the two layers is not well delineated and most investigators believe that these more cuboidal cells of the inner lining are only a more highly differentiated form of the connective tissue cells forming the outer layer. This inner layer is not infrequently thrown into pronounced folds which may be temporary formations depending upon the position of the joint, or they may form permanent villi which project into the cavity. Special emphasis is made at this point of the not uncommon tendency to villous formation. Later it will be shown that the majority of cases in

this series present a pathologic pattern which might well be described as a distorted attempt at villi formation.

As early as 1910, Lejars and Rubens-Duval[2] made the first real contribution to the classification of these tumors. According to these writers, there may be two types of malignant tumors arising from these structures depending upon what part of the capsule or tendon sheath the tumor takes its origin. If the cells develop from the fibrous layer, one cannot distinguish the tumor microscopically from the common fibrosarcoma, but if it arises from the inner layer whose cells, as noted previously, are more epithelioid in character, the pattern may strongly suggest synovial tissue as the origin of the tumor. It behooves the surgeon, therefore, to make careful note of the anatomic relationship of the tumor at the time of operation, as this may be of material aid in differentiating between the fibrous type of synovial tumor and the more common fibrosarcoma. It is probably because of this failure that all of the cases of this series belong to the second or synovial group, and undoubtedly those arising from the fibrous layer were simply classified as fibrosarcoma.

In making the diagnosis in the nine cases comprising this series, the history, clinical features and pathologic appearance have all been taken into consideration. In practically every incidence there has been uniformity of opinion among the pathologists to whom sections were submitted, otherwise the case was not included.

Incidence.—The study of previously reported cases of synovioma discloses a tendency for this type of tumor to occur between the third and fifth decades. With one exception, this was borne out in this series. The age of two cases was 17, and the remaining seven were between 21 and 42. Four were male, and five were female. All of the patients in this series were white.

Duration of Symptoms.—In this entire group of cases, swelling was the initial symptom. The time interval from the discovery of the swelling until medical consultation varied from three months to six years, the average being approximately two years. This, in itself, would indicate that pain was not an outstanding feature.

Pain.—Five of the nine cases complained of pain at the time of their first examination. In only one, however, was it described as severe.

Trauma.—A history of previous injury to the affected part was obtained from three patients, but in each it was relatively mild. The earliest development of a tumor following injury was three months.

Tumor.—The size of the swelling on examination varied between that of an olive and a hen's egg. It is interesting to note that in five cases the character of the tumor was described as cystic.

Location.—The tumors occurred most frequently in a lower extremity. Five developed about the knee, two arose from the region of the external malleolus, and one was located on the plantar surface of the foot. The remaining case originated on the right forearm near the elbow.

Roentgenographic Examination.—Roentgenographic studies revealed the shadow of a soft tissue tumor, but no bone involvement in any of the cases.

Operative Findings.—Unfortunately, in the majority of the cases the descriptions of the operative findings were very meager. Of the nine cases, three were reported as being encapsulated grossly. In three instances, the attachment to tendon sheaths was noted. The tumor, in one case, completely filled the suprapatellar and popliteal bursae and invaded the joint cavity at two points. Although the microscopic sections in a majority of the cases would indicate the rather vascular nature of the tumors, no observations were made at operation which would bear this out. Two cases were of particular interest in that the tumor removed at first operation was reported as a benign cyst.

Gross Pathology.—The gross examination of the specimens revealed one uniform finding—in all there was a tendency to cyst formation. In some, however, it was very pronounced, whereas in others this feature was less marked. The cysts contained either straw-colored or bloody fluid and one might suspect that the tumor cells continue the highly specialized secretory function of the parent synovial cell.

In general, the tumor was described as being poorly encapsulated, although as previously noted there was a definite capsule in three cases. The tumor itself was usually lobulated and soft in consistency. In one instance where the tumor was quite large, there were gross areas of necrosis. Their color varied from a grey to a faint yellow. In the one case where a metastatic inguinal node was removed for study, its gross appearance conformed to that of the original tumor.

Microscopic Pathology.—The striking similarity in the histologic pattern of the majority of the cases herein reported should demand special emphasis. Since 1910, when Lejars and Rubens-Duval first classified malignant joint tumors, observers have noted, from time to time, the peculiar epithelioid-like cuboidal cell which is so characteristic of these tumors. They have pointed out their probable relationship to the mesothelial lining cells of the joint cavities, bursae and tendon sheaths. Here, however, their analogy has stopped. This investigator was struck by the tendency of these tumors to form a papillary pattern which is not unlike the papillary projections found in villous arthritis. It is hardly possible that there is any etiologic association, yet, in synovioma we seem to have an attempt to form villi. In six of the nine cases of this group this pattern is found throughout the entire tumor, while in the others, although present, it is only seen in part of the section. Frequently the small cysts noted in the gross reveal, on microscopic examination, papillary buds projecting into the cyst lumina. The central portion of the papillary projections is composed of a stroma of fairly typical fibroblasts. Blood vessels are numerous. This central framework is covered by a layer of cells of a more cuboidal type with large vesicular nucleus and acidophilic cytoplasm. The thickness of this layer may vary from one to three cells, but there is no sharp line of demarcation between these larger cells and the more fibroblastic cells which form the stroma. In the spaces between the projections, there may be clear pink-staining fluid, and often hemorrhage is present. Where the

cells are more densely packed and the papillary formation is absent, the two types of cells described above may be found lying in adjacent bands. Mitotic figures are present but not numerous.

CASE REPORTS

Case 1.—Acc. 46896: E. D., a white, female, age 17, with synovioma in the region of the external malleolus of the right ankle.

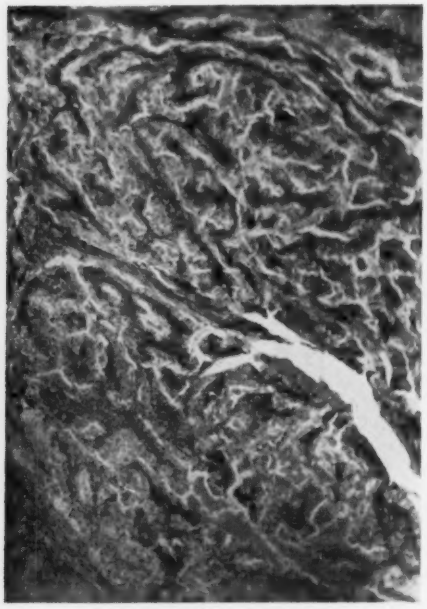

FIG. 1.—Case 2: Synovioma showing papillary arrangement of cells. (×100)

History.—In 1933, four months before admission to the hospital, the patient received a mild blow on the external surface of her right ankle. No significance was attributed to the injury until a small lump developed at this site. It was described as soft and cystic, approximating the size of an olive. Following excision by her physician, the wound failed to heal until the patient was given roentgenotherapy four months later. In 1934, there was a local recurrence of the tumor. A biopsy, made at this time, was reported as an angiosarcoma. Under further roentgenotherapy, the tumor again disappeared only to return again a year later.

Examination.—At the site of the operation there were several small pea-size nodules which were soft in consistency. These appeared to be adherent to the skin. There was no swelling of the joint itself. In the right inguinal region, there was an enlarged lymph node the size of a hen's egg.

Operation.—Excision of inguinal node.

Pathologic Report.—Macroscopic: A soft oval tumor about 4x3x2 cm., which on section showed a pale grey homogeneous surface with small cystic areas containing blood. *Microscopic:* A richly cellular tumor which for the most part is composed of closely packed polyhedral cells with large vesicular nuclei. Mitotic figures are common. There are several areas of hemorrhage and necrosis. Numerous small cysts are present which are lined by cuboidal cells and show papillary projections.

Subsequent History.—Patient received extensive roentgenotherapy to right ankle and inguinal regions. In 1936, examination disclosed an ulcer at the site of the original lesion. Two years later she developed evidence of pulmonary metastases, and died April, 1938. No autopsy was obtained.

Case 2.—Acc. 37019: E. A., a white, female, age 45, with synovioma in the region of the attachment of the biceps femoris tendon.

History.—Four years prior to her admission to the hospital, the patient first became aware of a swelling on the lateral surface of her left leg just below her knee. There was no history of previous trauma. The growth slowly increased in size until it was as large as a hen's egg. It was moderately painful to pressure.

Examination.—A smooth, soft tumor, 6x4x4 cm., was found on the lateral surface of the leg about the level of the head of the fibula. The tumor seemed attached to the deep structures, but the skin over it was freely movable. There was no swelling of the joint. Some tenderness could be elicited on moderate pressure over the tumor. Roentgenograms showed no evidence of bone involvement.

Operation.—March, 1932, a tumor, which seemed to arise from the biceps femoris tendon, was excised.

Pathologic Report.—Macroscopic: A well encapsulated, firm tumor which on section appeared to be lobulated. There were no cystic areas present. The cut surface was a dull grey with occasional areas of hemorrhage. *Microscopic:* A rather vascular tumor which displays mainly two types of cells with a marked tendency to papillary formation (Fig. 1). The fibroblastic or spindle-shaped cell seems to form a basement membrane for these projections, and the more cuboidal type of cell comprises the outer layer which

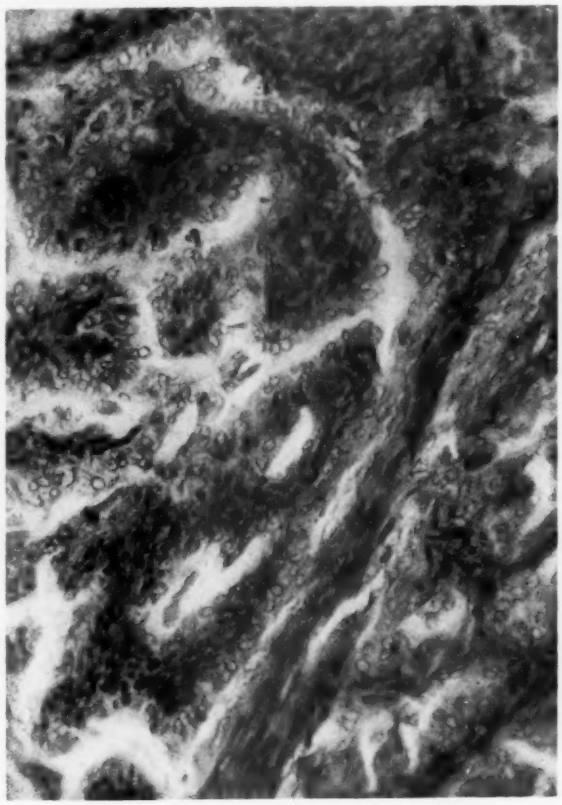

FIG. 2.—Case 2: The basement membrane of fibroblasts covered by the more typical cuboidal cell. (×400)

varies from one to four cells in thickness (Fig. 2). These cells show a vesicular nucleus. Some of the spaces between the papillary projections are filled with hemorrhage.

Subsequent History.—Following operation, the patient received intensive roentgenotherapy at the Walter Reed Hospital. In June, 1939, seven years after discharge from the hospital, the patient reports that she is well and has had no evidence of a local recurrence of the tumor.

Case 3.—Acc. 39605: M. D., a white, female, age 30, with synovioma developing on the plantar surface of the left foot.

History.—In 1930, the patient had what was thought to be a simple benign cyst excised from the plantar surface of the left foot. The duration of symptoms prior to this operation was not given, but two and one-half years after it a swelling developed at the

site of operation and slowly increased in size causing local pain and discomfort on walking.

Examination.—On the plantar surface of the left foot lying beneath the scar of a previous operation, there was a flattened, lobulated tumor just proximal and lateral to the base of the great toe. It was not attached to bone or to the overlying skin. Roentgenologic examination was negative.

Operation.—March 3, 1933, a lobulated nonencapsulated tumor, 3x1.5x1.5 cm., was excised from the region of the base of the great toe. It lay beneath the plantar fascia.

Pathologic Report.—Macroscopic: No description given. *Microscopic:* The picture presented here is identical to that of Case 2. Characteristically, the epithelioid type of cell is found overlying those more spindle in appearance. The papillary structure is equally pronounced. (Figs. 3 and 4).

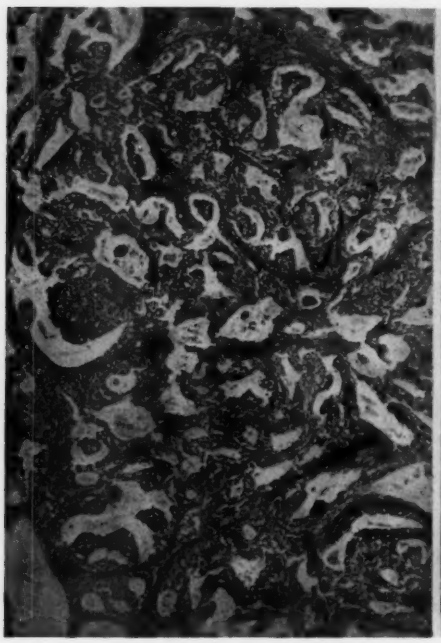

FIG. 3.—Case 3: Synovioma with the typical papillomatous pattern. (×100)

FIG. 4.—Case 3: High magnification to show villous-like structure so characteristic of the entire tumor. (×500)

Subsequent History.—Following operation, the patient received a course of roentgenotherapy, but in 1935, two years later, the tumor recurred and grew rapidly. At reoperation it was found to involve most of the tendon sheaths on the plantar surface of the foot. Further roentgenotherapy was given, with only temporary benefit, and, in 1937, the foot was amputated because of extensive ulceration of the plantar surface. Two months later she developed an inguinal mass. Her course from this point was steadily downhill, with death from pulmonary metastases in December, 1938.

Case 4.—Acc. 60073: V. S., white, female, age 22, with synovioma developing in the region of the left ankle.

History.—Two and one-half years before admission to the hospital, the patient fell, striking her left ankle. A slight swelling, which was not particularly painful at first, developed several months later and at the end of two years it had increased noticeably in size.

Examination.—Below the internal malleolus of the left ankle, and extending on to the plantar surface of the foot along the longitudinal arch, there is a soft cystic swelling. The area over the tumor was exquisitely tender. Roentgenograms were negative for any bone involvement.

Operation.—On October 10, 1938, a tumor was excised which extended from the os calcis to the heads of the metatarsals beneath the plantar fascia. It was described by the operator as being well encapsulated and extremely vascular. There was no contact with any bony structure.

Pathologic Report.—Macroscopic: A granular, greyish mass with occasional yellow spots, but no definite cystic areas. As the tumor had not been removed in one piece,

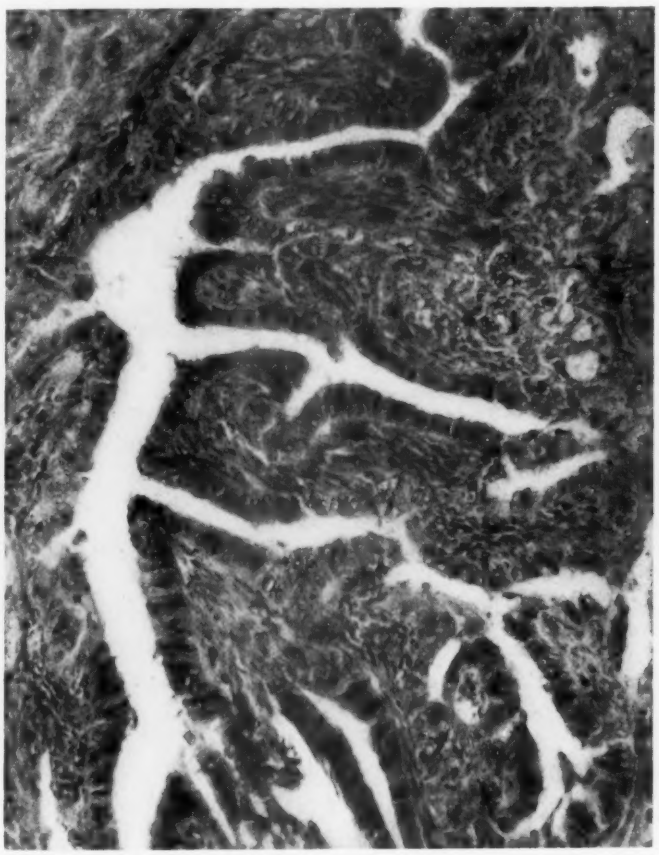

FIG. 5.—Case 4: Synovioma illustrating again the papillomatous structure.

it was difficult to state how completely it had been encapsulated. *Microscopic:* A highly vascular tumor which shows the typical papillary pattern. These papillae have a framework of elongated spindle cells and are covered by cells which closely resemble columnar epithelium (Fig. 5). In some fields the line of demarcation between these two types of cells is striking, but more commonly the epithelioid cells fade into the spindle-shaped cells without any sharp line of division. Mitotic figures are not prominent in this tumor.

Subsequent History.—Following operation, the patient received radiation therapy. On examination, 18 months later, she appeared in an excellent state of health, with no evidence of local recurrence of the tumor.

Case 5.—Acc. 50530: W. V., a white, male, age 45, with a synovioma of the left thigh five inches above the knee.

History.—In 1933, the patient first noticed a swelling on the medial surface of his left thigh just above the knee. The tumor at this time was about the size of a half dollar and seemed to be superficial. It grew gradually until two weeks before admission to the hospital when it appeared almost to double its size in ten days. This was accompanied by some pain which radiated down his leg. No history of previous injury could be obtained.

Examination.—On the medial surface of the left thigh, five inches above the knee, there was a mass the size of a hen's egg which was firm, warm, somewhat tender, and apparently not fixed to the skin or underlying tissues. Roentgenograms were negative except for soft tissue swelling.

Operation.—On June 29, 1936, the tumor was found to have invaded the popliteal space and to surround the femoral vessels. A diagnosis of fascial sarcoma was made and immediate midthigh amputation was performed.

Pathologic Report.—Macroscopic: A large oval, lobulated mass with attached muscle and fat, which measured 11x9x8 cm. The tumor was not well encapsulated and its sectional surface was variable in appearance. Some of the lobules were soft, homogeneous and grey, while others were yellow. No definite cysts were described. The centers of some of the lobules were almost caseous in consistency. *Microscopic:* Both typical types of cell are present in the sections studied, but the epithelioid type predominates. So closely packed are they in some places that the usual pattern is missing. Elsewhere, however, a papillary arrangement is presented. In several areas the cuboidal-shaped cells form acinous-like structures which contain pink-staining material. Mitotic figures are frequent and in some areas there are small clumps of foam cells. Where the margin of the tumor is shown, it is obviously invasive.

Subsequent History.—The patient has been seen at regular intervals since his operation. At his last examination, January 24, 1939, he complained of pain in his stump, but there was no evidence of local or distant metastases.

Case 6.—Acc. 40595: C. K., white, male, age 17, with a synovioma arising on the left forearm near the elbow.

History.—Four months prior to admission to the hospital, the patient noticed a painless swelling on his left forearm that rapidly increased in size.

Examination.—A soft, well circumscribed, cyst-like mass the size of a hen's egg which, before operation, was diagnosed as a benign cyst.

Operation.—Local excision, June, 1933.

Pathologic Report.—Macroscopic: An irregular lobulated mass which was thought by the operator to arise from a tendon. The tumor was poorly encapsulated. It was yellow in color and contained numerous small cystic areas filled with clear fluid. *Microscopic:* The tumor, which is extremely cellular, is composed of interlacing bundles of plump spindle cells. There is a tendency to cyst formations which are lined by a more cuboidal-shaped cell. Conspicuous in some of these small cyst cavities are papillary projections.

Subsequent History.—The patient received a short course of postoperative radiation. A year later, June, 1934, a recurrent mass the size of a large cherry was excised. It presented the same pathologic appearance as the original tumor. He has been examined yearly, and, in January, 1939, was reported well, without evidence of local or distant metastases.

Case 7.—Acc. 43768: E. H., white, female, age 35, with a synovioma involving the right knee.

History.—Seven years before admission to the hospital, the patient struck the outer surface of her right knee. The area remained sensitive to pressure and a year later a pea-size nodule was noted. There was a progressive increase in size of the tumor ex-

tending into the popliteal space and limiting motion of the knee joint 50 per cent. Pain was not an outstanding symptom.

Examination.—The right knee was one-third again its normal size. The enlargement was due to a firm irregular tumor composed of two almost distinct parts, one on the anterior lateral surface and a second filling the popliteal space. Fluid also could be demonstrated in the joint. Roentgenologic studies were negative for bone involvement and lung metastases.

Operation.—Biopsy, followed by midthigh amputation in July, 1934.

Pathologic Report.—Macroscopic: The tumor was moderately well encapsulated, almost filling the suprapatellar and popliteal bursae. At several points it had invaded the joint cavity. The tumor was made up of lobules of rubbery consistency which showed occasional cystic areas. No bone involvement could be demonstrated. *Microscopic:* Sections did not show the typical papillary arrangement which characterized the preceding cases. The tumor was comprised of closely packed round or oval cells with little or no visible cytoplasm. The nuclei were vesicular with occasional nucleoli. In sections from other portions of the tumor, the cells form a lace-like pattern and are more spindle-shaped in character. Numerous small blood vessels indicate its vascularity and mitotic figures are quite numerous.

Subsequent History.—Following operation, the patient had intensive roentgenotherapy, but five months later pulmonary metastases could be demonstrated. Her course was rapidly downhill, with death occurring in June, 1938.

Case 8.—Acc. 54821: G. S., white, male, age 25, with a synovioma arising in the left popliteal space.

History.—In July, 1936, three months before admission to the hospital, the patient developed a small lump in the left popliteal region which slowly increased in size. The tumor was thought, clinically, to be a bursal cyst and was excised. Pathologic report of specimen was "benign cyst." Shortly after operation, the swelling recurred and increased rapidly in size to involve the entire popliteal space. He was readmitted to the hospital in December, 1936, because of pain, swelling and loss of motion in his left knee.

Examination.—Filling the left popliteal space was a firmly fixed tumor which gave the impression clinically in certain areas of being cystic. Flexion of the knee was limited to 60°. Pressure over the mass produced very little pain. Several small nodes were palpable in the left inguinal region. There was no evidence of bone involvement roentgenologically.

Operation.—December 5, 1936, the popliteal region was explored. A poorly encapsulated tumor was found which measured 15x7x5 cm. and completely filled the popliteal space. At one point it appeared to be attached to the periosteum of the tibia. The popliteal vessels were completely surrounded by the tumor, which was obviously infiltrating in character, making surgical removal impossible. A specimen was excised for study.

Pathologic Report.—Macroscopic: No record made. *Microscopic:* The sections show a cellular tumor made up for the most part of spindle-shaped cells. In areas the cells are densely packed and form in whorls, while in others they lie in looser tissue and give a lacey, myxomatous appearance. Papillary formation is not striking, but there are cystic areas which are lined by more cuboidal cells. Mitotic figures are numerous.

Subsequent History.—Following operation, the patient's course was rapidly downhill, with death occurring April 16, 1937, four months later. At autopsy, metastases were found to the inguinal nodes and both lungs. A note on the gross appearance of the tumor at this time is of interest. It is described as displaying numerous small cystic areas which contained a sticky, glairy mucoid fluid.

Case 9.—Acc. 58089: A. S., white, male, age 27, with a synovioma developing in the left popliteal space.

History.—Five weeks prior to admission to the hospital, the patient first observed a small lump in the left popliteal space. There was no history of previous injury. The

tumor steadily increased in size and although there was no real pain, the patient complained of a constricting sensation in this region.

Examination.—Superficially placed in the left popliteal space there was a fluctuant mass, 5x6x3 cm., which was not attached to the skin or the underlying structures.

Operation.—Excision of cyst under local anesthesia April 21, 1938. There was no apparent communication with the joints.

Pathologic Report.—Macroscopic: The cystic tumor is the size of a lemon and contains a chocolate-colored fluid. The capsule is 3x4 Mm. in thickness, and its inner lining has a sulphur-yellow color. *Microscopic:* The capsule consists of fibroblastic tissue with numerous small blood vessels and scattered collections of hemosiderin. The inner lining is composed of more cuboidal cells varying from three to five cells in thickness. Papillary projections are numerous. Occasional giant cells of the epulis character are present.

Subsequent History.—One year following operation, April, 1939, a marble-size tumor developed at the site of the original lesion. This gradually enlarged to the size of an egg and, in July, 1939, it was excised. The operator again described the tumor as cystic in character. Pathologic studies revealed a picture similar to that of the original tumor, but with a greater tendency to papillary formation. In February, 1940, the patient reported a second recurrence for which he is now under observation. Amputation was refused by the patient. He is now receiving radiation therapy.

Diagnosis.—In none of the nine cases included in this report was a correct preoperative diagnosis made. The clinical impression in five cases was benign bursal cyst. There is really nothing characteristic about the history or clinical appearance of synovioma. It is, therefore, of highest importance that detail gross and microscopic pathologic studies be made in all cases of tumors removed from joints or regions adjacent to bursae and tendon sheaths. Cursory routine examination led two cases to be overlooked by the pathologist, who made the diagnosis of benign bursal cyst. The correct diagnosis was not made until a recurrent tumor was explored.

In most cases the gross and microscopic appearance of the more common xanthoma or giant cell tumor would quickly differentiate it from synovioma. Gunnar Jonson,[3] in reporting a series of cases treated at the Radiumhemmet, Stockholm, points out the possibility of confusing synovioma with a chronic villous arthritis. In fact, two of his cases were so diagnosed at operation. The more diffuse character of this lesion, together with pathologic studies (Fig. 6), should establish the correct diagnosis. Whenever a cystic tumor is removed from a region where a bursal cyst may arise and is found to contain chocolate-colored fluid rather than the usual clear gelatinous fluid common to such a cyst, the possibility of a synovioma must be considered. Should microscopic studies reveal a cellular lining with papillary formations in contrast to the flat single cell lining of a bursal cyst, the diagnosis of synovioma is established.

Treatment.—No dogmatic statement can be made regarding the management of synovioma based upon so small a group of cases. From a review of the literature one is left with a very pessimistic outlook, regardless of the therapy employed. This does not seem entirely justified if we analyze the results of the nine cases herein reported. The mortality rate of 45 per cent is misleading if we do not consider that the treatment in three of the four

TABLE I

RÉSUMÉ OF NINE CASES OF SYNOVIOMA

Case No.	Age	Sex	Duration Before Operation	Symptoms	Location	Operation	X-ray Therapy	Results
(1) E. D. Acc. 46896	17	Female	4 months	Soft cystic, olive-size tumor	External surface of right ankle	Excision 1933	Yes	Recurrence 1 yr. later, with inguinal metastases. Death from pulmonary metastases, 1938
(2) E. A. Acc. 37019	45	Female	4 years	A slowly growing, moderately painful, egg-size tumor	In region of head of left fibula	Excision 1932	Yes	Living and well, without evidence of recurrence, June, 1939
(3) M. D. Acc. 39605	30	Female	2½ years	Swelling, with local pain and discomfort on walking	Plantar surface of left foot	Excision 1933	Yes	Recurrence 2 years later. Further X-ray therapy followed by amputation. Death from pulmonary metastases, 1938
(4) V. S. Acc. 60073	22	Female	2½ years	Gradual development of painless swelling	Below internal malleolus of left ankle	Excision 1938	Yes	Well, without evidence of recurrence 18 months following operation
(5) W. V. Acc. 50530	45	Male	3 years	Gradual swelling, with slight pain	Medial surface of left thigh just above knee	Midthigh amputation 1936	No	Living and well 4 years after operation
(6) C. K. Acc. 40595	17	Male	4 months	Painless, egg-size swelling	Left forearm near the elbow	Excision June, 1933	Yes	Recurrence 1934. Second excision. Living and well 7 years later
(7) E. H. Acc. 43768	35	Female	7 years	Gradual enlargement of tumor, limiting junction of knee	Right knee	Midthigh amputation 1934	Yes	Death from pulmonary metastases, 1938
(8) G. S. Acc. 54821	25	Male	3 months	Gradual development of small cystic tumor	Right popliteal space	Excision 1936	No	Extensive recurrence within 4 months, and death from pulmonary metastases 5 months later
(9) A. S. Acc. 58089	27	Male	5 weeks	Painless swelling	Left popliteal space	Excision 1938	Yes	Now under treatment for second recurrence

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patients who died was totally inadequate. In two of the cases which terminated fatally, the correct diagnosis was not made until the tumor recurred, and even then only local excision was attempted at the second operation, although it must have been obvious that the tumor could not be com-

FIG. 6.—Photomicrograph to show pathologic pattern of a typical case of villous arthritis.

pletely removed without destroying vital structures. A third case, which died, did not seek medical aid until the tumor had grown over a period of seven years from the size of a pea to double the size of the knee. It is not surprising that pulmonary metastases were noted in this instance, five months after a midthigh amputation. In the fourth fatal case, an incorrect diagnosis of a benign cyst was made at the first operation, and when examined four months later the tumor had already metastasized. This case is unique in this series because of its fulminating course.

Of the five surviving cases, four have been treated by local excision followed by radiation. Three of these are living and well, two, seven and eight years, respectively, after their operation. In the fourth case, two recurrences have developed during a period of two years. The fifth patient is apparently in good health, four years after a midthigh amputation for a tumor of the popliteal space which could not be completely removed without injury to the popliteal vessels.

We may conclude from the above that the prognosis in synovioma is not as poor as the literature would lead us to believe. Conservative treatment of these tumors along the following lines seems warranted: Wherever the tumor can be completely excised with a margin of healthy tissue and appears encapsulated, this should be the method of choice. Where the tumor cannot be removed completely without injury to important structures, amputation should be performed.

The effect of radiation therapy is, as usual, difficult to evaluate, but it would seem a plausible adjunct to surgery where the tumor has been excised. In this series, however, where inguinal metastases have developed, or there has been a local recurrence, it has not seemed to have had any effect on the ultimate outcome.

Course of the Disease.—One conclusion we can definitely draw after a study of these cases is that the rate of growth is slow and metastases appear late in the disease. There was only one exception, the patient who died within nine months of the time when the lesion was first noticed. The other three who progressed to a fatal termination lived five, seven and ten years, respectively, after the onset of symptoms. During the course of the disease three of the four patients who died developed metastases to the inguinal nodes, and at the time of death all showed pulmonary involvement.

CONCLUSIONS

(1) A series of nine cases is reported.

(2) Two distinct types of tumors may arise from synovial-lined structures depending upon what part of the capsule they take their origin. From the outer or fibrous layer, tumors develop which are indistinguishable from the common fibrosarcoma. From the inner or synovial lining of the capsule, cystic tumors may arise which have a characteristic papillomatous pattern. All of the cases of this series fall into this latter group.

(3) Grossly, the tumors may be composed of single or multiple cysts which, microscopically, reveal a typical villous structure of fibroblastic cells covered by cuboidal mesothelium.

(4) In view of the absence of any specific diagnostic clinical features of synovioma, the importance of careful pathologic studies has been stressed.

(5) In the improperly diagnosed and inadequately treated cases, the course is protracted and uniformly fatal.

(6) Based upon a study of the cases of this series and those reported in

the literature, a plan of treatment is proposed which, in the light of our present knowledge, would seem both rational and conservative.

I wish gratefully to acknowledge the assistance in the preparation of this paper of Lt. Col. J. E. Ash, U.S.A., Curator of The Army Medical Museum, Washington, D. C. Upon his pathologic studies, this paper is largely based.

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CHOICE OF BONE GRAFT METHODS IN BONE AND JOINT SURGERY

RALPH K. GHORMLEY, M.D.

SECTION ON ORTHOPEDIC SURGERY THE MAYO CLINIC

ROCHESTER, MINN.

DURING THE YEARS which have passed since the introduction of modern surgery, many methods of bone grafting have been advocated, each with a plausible explanation of its use. Many of these procedures have not stood the test of time. However, a review of those available to-day reveals a surprising number of useful methods.

There may be wide differences of opinion as to the choice of method to be used under certain conditions, and several may be adaptable. Much depends upon the experience of the individual surgeon with each type of procedure.

There are available, now, for use in bone graft surgery three essential types of graft: (1) Autogenous grafts, in which the bone is removed from one part of the patient and transplanted to another part of the same patient; (2) homogenous grafts, in which bone is removed from another person such as a relative and transplanted to the affected part of the patient; and (3) heterogenous bone transplants, in which bone from another species is used in transplantation. Usually this is some type of beef bone though bones of other animals have been used. These may be subdivided as in Table I.

TABLE I

CLASSIFICATION OF TYPES OF BONE GRAFT

Autogenous grafts:
- (1) Cortical bone (usually tibia)
- (2) Cancellous bone (usually iliac crest and wall)
- (3) Osteoperiosteal bone (usually tibia)
- (4) Fibula or rib (combining the foregoing)
- (5) Chip-grafts, shave-grafts, *etc.*
- (6) Delayed grafts

Homogenous grafts:
- (1) Cortical
- (2) Cancellous
- (3) Any other type tabulated under autogenous grafts

Heterogenous grafts:
- (1) Entire bone
- (2) Cortical } "*os purum*"
- (3) Cancellous }
- (4) "*Os novum*"—combination of heterogenous and autogenous grafts

There may be variations in the type of graft from the standpoint of its placement at the site of transplant, such as: (1) Onlay; (2) inlay; (3) intramedullary; and (4) wedge—variation of inlay.

In deciding what type of graft is to be used several factors must be taken into consideration:

If the graft is to serve as a fixative agent as well as to furnish osteosynthesis, cortical grafts of some type must be used.

In some instances in which the shearing force may be great and external fixation inadequate, as in ununited fractures of the neck of the femur, a stronger graft than the simple tibial cortical graft may be necessary and a fibular graft may be used. Where such a tubular bone is used, the strength of the graft is much greater and the graft will better withstand the shearing force mentioned.

Where defects in bone are to be filled, as in bone cysts, cancellous bone may be used, although in many cysts the capacity of the defect is such that it is necessary to resort to all the available sources and one may use both cancellous and cortical bone.

Where a definite plastic effect is desired, such as the making of a shelf over an inadequate acetabulum, the cancellous bone from the wall and crest of the ilium seems, to my colleagues and me, to be most adequate.

Where speed of union is important, the cancellous graft of some type is probably the best, for reasons to be demonstrated later, provided it is otherwise suitable.

It may be fairly well shown that all grafts go through certain stages between the time of transplant and the final result, which in many cases is not reached for several months or years after the transplant is done.

Once the transplantation operation is completed, there is about the graft a wall of blood clot which begins the usual stages of organization. During this process blood vessels form in the organizing tissue. If the graft is permeable enough, it may be invaded by the organizing connective tissue. If cancellous bone is used as a graft, this invasion by connective tissue is much more readily accomplished, as may be seen in the experimental grafts. If the graft is a cortical graft with some cancellous bone attached, the invasion by the connective tissue may take place more slowly, and where pure cortical bone is used this invasion is slower in direct proportion to the density of the bone.

After the circulation to the graft is established through the invasion by connective tissue, a stage of reduction in density of the graft begins and in some cases may proceed to such an extent as to make the graft extremely vulnerable. Fractures of grafts during this stage are not uncommon. However, with the completion of this phase and usually by the resumption of some active stress, recalcification and reossification of the graft take place and this process may go on to such a degree that, in the end, the mass of bone over the grafted area is two or three times as large as the original graft.

Hypothesis of Bone Growth.—The foregoing observations are taken from a series of experiments reported by Stuck and myself in 1934. At that time we summarized the hypotheses of bone growth into five groups:

(1) Growth and replacement of bone are brought about by specific osteogenic activity of the periosteum (Ollier, 1867).

(2) All of the transplanted bone dies and is replaced by proliferation of new bone from the surrounding host tissue (Barth, 1893).

(3) Replacement of bone grafts and repair of bony defects are effected by proliferation of bone from the periosteum and endosteum (Axhausen, 1908).

(4) The periosteum has no osteogenetic function. Bone grows and repairs itself by proliferation of bone chips (Macewen, 1912).

(5) New bone is formed by metaplasia of the preexisting connective tissue in the region where the bone is to be laid down (Baschkirzew and Petrow, 1912).

To this list may be added the views more or less attributed to Leriche and Policard, who stated that: "The problem of osteogenesis has passed through many phases. It has been histologic and surgical and at the present time it is, above all, chemical." These authors have elaborated an hypothesis that all formation of bone is the result of metaplastic change in the connective tissue where bone is to be laid down. There are three stages in this metaplasia: (1) Transplantation of connective tissue by edematous infiltration with multiplication of connective tissue fibrils; (2) infiltration by a special substance clinically undefined, the preosseous substance; and (3) deposit in that substance of a mixture of calcium phosphate and calcium carbonate, producing bone.

This view may be said to be largely theoretic until more knowledge of chemistry of body tissues and particularly of bone is gained. What such knowledge as the future may bring will do to support or modify this hypothesis is, of course, unknown. But with the rapidly increasing knowledge of chemistry as applied to medicine, it is probably safe to predict that at least a major part of the process of bone formation will be known to be purely chemical.

We have not by any means been able to demonstrate these steps in our experimental work. However, we feel that we have proved that grafts which are more readily permeable by granulation tissue unite more quickly with their host bone. The more compact grafts go through the same process but this takes a much longer time.

Cortical Grafts.—My colleagues and I use cortical grafts probably more widely than any other type. In treating ununited fractures of the long bones we use them almost exclusively. Here the splinting effect of a solid graft is most desirable. It is essential to fix the ends of the long bone by some means and fixation can be accomplished in this way. This applies to practically all of the ununited fractures of shafts. Cortical grafts are used as a rule in cases of scoliosis in which the deformity is not severe but in which a supporting graft of the "strut" type is desired. Cortical grafts may be used to fill large defects such as those seen in bone cysts. Bone grafts for tuberculosis of the spinal column and for spondylolisthesis are usually of this type.

Cancellous Grafts.—The cancellous type of graft may be used in lumbosacral bone graft operations in which only two vertebrae are to be fused, that is, the fifth lumbar vertebra to the sacrum or occasionally two other vertebrae. Such grafts are also adaptable in making shelves in the case of congenital dislocation or subluxation in which a shelving type of operation is desired. Such cancellous grafts are most adaptable in filling small and large bony defects such as are seen in bone cysts or giant cell tumors. In these cases oftentimes a large amount of bone is necessary to fill the defect and it may be necessary to use both cortical and cancellous bone in such instances. Cancellous bone, in

the form either of large flat shavings or of solid grafts from the ilium or trochanter, is often used as an adjunct in the various types of ankylosing operations on the hip.

Osteoperiosteal Grafts.—In our hands osteoperiosteal grafts are used only in cases of severe spinal deformity, such as are seen in advanced cases of scoliosis or tuberculosis, in which straight or slightly curved solid grafts cannot be made to fit.

Fibular Grafts.—In our hands fibular grafts are used almost exclusively in cases of ununited fracture of the femoral neck. In these cases the tibial cortical graft has been found to fracture rather late in the convalescence owing to the shearing force noted previously. Although fibular grafts may fracture, such fractures occur much less frequently than in tibial grafts. Another type of fibular graft is the so-called Huntington operation, in which the fibula is transplanted at either end to the remaining epiphyseal portions of the tibia and thus replaces the absent shaft of the tibia.

Rib Grafts.—Rib grafts have been used over a long period. Many of the earlier workers in bone graft surgery employed rib grafts. In our own experience they are now used for only one type of case, that is, scoliosis with severe deformity of the ribs. In these cases the ribs are resected to correct the deformity as much as possible and used as transplants to reinforce the fusion of the affected portion of the spinal column.

It is my impression that rib grafts are used in facial plastic surgery, which is out of our consideration here.

Chip-grafts and Shave-grafts.—From time to time various authors have recommended the use of chip-grafts and shave-grafts. These are very useful in filling bone cavities, in implanting in the area of fusion in the spinal column or as implants about a site of nonunion to furnish additional bone to the main graft. They usually are obtained from the tibia but also may be obtained from the ilium.

Match-grafts.—Small pegs of bone used in grafting small fragments of bone together, as in ununited fractures of the carpal scaphoid bone, are often called match-grafts. These are simply small cortical grafts and as such go through the stages of healing seen in any case in which cortical bone grafts are employed.

Delayed Grafts.—Brooks and Hudson have developed another method of bone transplantation in experimental animals and Key has adapted the method to operations on human beings. In the first stage the transplant is cut on the donor but not removed, and its bed is prepared. In the second stage, several days later, the transplant is removed and placed in its new bed. Key reported the use of this method on patients three times for nonunion with a successful result each time. Leriche and Policard stated that: "The take is more rapid and the osteogenesis of better quality. The biologic explanation of this fact is simple: The preliminary preparation leads to a rarefaction of the bone and consequently augments the permeability of the passageways for the rehabilitation."

Along this same line Leriche and Policard quoted the observation of

Chutro "that the bone graft unites better when the transplanted bone is affected by extensive trophic and nutritive disturbances. These disturbances result in a rarefaction which automatically increases the permeability."

These observations are all in accord with what has been noted already, namely, that the permeability of the graft makes for an easier invasion by the connective tissue which becomes the source of blood supply and ultimately is important in the healing and union of the graft.

Homogenous Grafts.—From time to time the use of bone from individuals other than the patient has been advocated. In instances in which persistent nonunion has occurred and for some reason, usually because of inadequate size or strength of the bone, the patient's tibia or ilium does not seem suitable as a donor area, grafts may be taken from another individual, usually a parent or close relative, although this relationship is not necessary. That this type of graft may be successful I know from personal experience. I have been unable, however, to obtain from the literature any definite facts regarding the relative success of this type of grafting as compared with autogenous grafting. In one article by Brooks and Hudson on the experimental use of homogenous bone transplants a statement is made that the homogenous graft was successful in 76.8 per cent of cases as against 84.8 per cent of autogenous grafts in the same type of animal. These authors stated that they did not study the reactions in the beds to which the grafts were transplanted. In several of the experiments the blood corpuscles and serums were tested for iso-agglutinins and hemolysins but none were demonstrated. Brooks and Hudson referred to work on transplantation of other types of tissue by Loeb, who found that syngenesioplastic transplantations were more successful than homogenous transplantations but less successful than autogenous transplants. By syngenesioplastic transplants is meant the use of transplants from closely related individuals as donors. So far as I have been able to ascertain, this has not been determined from clinical applications of the method.

Neuhof stated that "homoplastic grafting has not had extensive clinical application. Differences between the sera of two individuals is undoubtedly an important factor in the uncertainty of success attending its use, but this has only been considered theoretically and has not been proved experimentally."

Our experience with homoplastic bone transplantations at the clinic has been limited to 19 operations on 14 patients, with the results shown in Table II.

TABLE II

RESULTS OF HOMOGENOUS BONE TRANSPLANTS IN 19 OPERATIONS UPON 14 CASES

	Number of Operations	Success	Failure	Unknown
Donor: Father, mother or brother	13	7	6	0
No relationship	6	3	2	1
Total	19	10	8	1
Blood-matching recorded (cases)*	5		4	1

* Three of these cases were of congenital pseudarthrosis. All donors were parents.

Thus, from our own experience at the clinic it cannot be said that the donor should be a close relative or that the blood should be matched. In one case a piece of bone from a donor not related was preserved in alcohol for a time

before being used successfully as a graft. Such experiences have been reported in the literature from time to time. Although by no means to be recommended as a routine procedure in bone grafting operations, homoplastic transplantation does have a place in the occasional case in which bone is desperately needed and for some reason or other the patient is in no condition to withstand autotransplantation.

Perhaps more efforts at blood-matching in our series would establish the importance of this procedure, but from these cases studied there is little to offer as an argument in favor of it.

In an emergency one may employ bone from an amputated limb, provided the condition of the amputated part is such that there is no danger in its use. The presence of infection, malignant lesion, *etc.*, would, of course, forbid the employment of such material for grafting purposes. The material may be preserved for a time in alcohol or ether without destroying its value as a graft. One must approach such a procedure without promising too much to the patient, but under conditions of extreme necessity such methods may be used with some assurance of success.

Heterogenous Transplantation.—The use of bone from other species than man has been reported from time to time with varying statements of success.[8] Such materials as beef bone screws, plates and grafts have been employed for many years and are still in rather general use, with perhaps some increased stimulation by the work of Orell which has received widespread publicity during the past few years. Besides advocating the employment of specially prepared beef bone, Orell has recommended the use of what he calls *"os novum."* In this procedure a strip of beef bone is implanted subperiosteally over the anteromedial surface of the tibia. One to two months later the implant together with the newly formed bone surrounding it is transplanted to the desired bed.

The method seems to have gained some popularity, particularly in Europe, if one is to judge by various reports in the European literature. How extensively it may be used in this country I cannot say at this moment. My colleagues and I have used beef bone screws for years. This method of fixation of autogenous grafts has been advocated by Henderson. It has proved a very satisfactory method of fixing grafts. Occasionally there may be some evidence of reaction around the screws and their extrusion may be noted or their removal may be necessary. For this reason my colleagues and I have lately been using vitalium screws to fix our bone grafts. Whether or not they will prove more satisfactory than beef bone screws is as yet to be demonstrated. They have apparently been satisfactory to date.

Beef bone plates were used for some years, usually as a method of fixation of fresh fractures. As such they proved satisfactory in some cases but the fact that they are no longer used attests to the preferability of other means of internal fixation over them.

Other types of heterogenous bone transplant reported in the literature have been bone from rabbits, sheep, chickens and monkeys,[12] eye teeth of

walruses, stags' antlers[7] and beef horns. This is undoubtedly only a small list of the materials used, as others are recorded in fragmentary case reports such as the successful transplantation of the tibia of a freshly killed goat.[8] All of this simply shows that again one may, under extraordinary circumstances, employ various types of heterogenous bone as a grafting material. Actually, my colleagues and I feel that the circumstances must be extraordinary to justify the use of heterogenous bone and that for the routine employment of bone grafting methods one should use autotransplants.

Postoperative Complications.—Once the transplant is completed, probably the greatest source of failures is through infection. Many rules may be made about the time to operate after all infection has apparently subsided in a compound fracture. Various intervals of from six months to two years—have been advocated as necessary before attempting bone grafting operations. One cannot, of course, ever be sure. It seems to me more important to attempt to determine whether there has been a very active type of infection and, if so, whether there has been serious damage to the surrounding soft parts so that much dense scar tissue is present. One can usually deal with the scar tissue between the ends of the bone fragments by excision. If the soft tissues around the fragments are severely scarred, however, serious impairment to the healing of the graft may result. If infection develops about the graft as the result either of a flare-up of an old infection or of introduction from elsewhere, one must determine, first of all, whether the infection is a localized one, which may cause little or no general reaction, or whether a serious general reaction is taking place. In the latter case, free drainage of the wound may be necessary, combined with whatever general measures may be indicated. In milder, localized infections the utmost consideration must be used in the care of the wound. By such treatment oftentimes a satisfactory union may be obtained and thus a good result salvaged from what may have appeared to be at first a failure. Oftentimes a graft may live in part through such an episode and sufficient normal bone may be formed to promote a good union or whatever effect may be desired from the operation.

Fractures of grafts may occur and, under some circumstances, such a complication may prove serious. This is particularly true where the graft is used to repair an ununited fracture. However, continued external fixation may produce union of the graft through the fractured area and a good result may thus be obtained. In the case of grafts to the spinal column it has been my observation that, as a rule, the strut-graft for scoliosis will unite and be even stronger at the site of fracture. On the other hand, a graft for tuberculosis of the spinal column may fracture and fail to unite, with a resulting failure of the operation. In the former case the constant friction of the ends of the graft may promote union. In the latter case the tendency is for distraction of the ends of the graft to take place with resulting failure of union.

The ultimate fate of grafts, once they are firmly united, is usually to remain *in situ* and, if put to mechanical stress, to increase in size and thickness over two or three years. Occasionally absorption may take place without any

definite known cause, possibly in some instances as a result of a negative calcium balance. In general, the character of cortical bone and cancellous grafts will be maintained.

CONCLUSIONS

(1) Bone grafts must become attached to the host by granulation tissue.

(2) This granulation tissue must invade the graft.

(3) In the case of cortical grafts, this invasion will be delayed because of the relative impermeability of the graft.

(4) During this period the graft may undergo apparent death of a varying degree of completeness.

(5) After vascularization the graft may appear to atrophy owing to the increased circulation.

(6) During this period of transformation and reduced density grafts are more fragile than during other periods and may fracture easily.

(7) Ultimately both cortical and cancellous grafts become restored to normal consistency.

(8) Over a period of years most grafts will become thicker and heavier as they are subjected to stresses and strains.

(9) Dead bone may ultimately become revascularized and replaced by new bone, witness disappearance of beef bone screws in grafts. Sometimes the continued presence in roentgenograms may be an indication of "retarded bone metabolism."

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INTERINNOMINO-ABDOMINAL AMPUTATION *

CASE REPORT

ALFRED H. WHITTAKER, M.D.,
AND
DAVID J. SOBIN, M.D., M.S.
DETROIT, MICH.

IN 1935, G. Gordon-Taylor and Philip Wiles[1] published the record of their five cases of hind quarter resection, together with an exhaustive summary of the current literature. Altogether there had been 79 cases reported, with 46 deaths, a mortality of 59.5 per cent. They were able to verify 55 of these cases of which 31 (56.4 per cent) died; of these 55 cases, 37 had been amputated for malignant disease of the lower extremity, with 20 deaths (54.1 per cent); 15 for tuberculosis, with ten deaths (66.6 per cent); one for nontuberculous disease of the hip, which lived, one for osteoclastoma, which was living some five and one-half years later, and one for an unknown cause, which died. Since 1935, 15 cases have been reported in various periodicals in different countries (Table I), of which Gordon-Taylor[2] has contributed six of his own. Six (40 per cent) of these 15 cases died within variable periods of elapsed time—as long as six months. Of the ones that lived, one had been operated upon five years ago, another three years, three of them for a few months, and of the remainder all we know is that they survived operation. The purpose of this paper is to present the history and subsequent course of a case of successful hind quarter amputation.

The indications for this radical procedure are[3]:

(1) Extensive disease of the proximal thigh, where disarticulation of the hip will not suffice for complete eradication of the disease. This may be malignant or benign.
   a. Bone tumors involving the proximal end of the femur, the pelvic bones, or extending into the soft parts of the pelvic cavity.
   b. Chronic bone infections in the same locality not yielding to surgical drainage.
   c. Malignant tumors or infections of the soft parts of the hip area, extending into the bones or into the tissues of the buttocks.

(2) Malignant bone tumors of the ilium and tumors of the soft parts of the pelvis too extensive to yield to local resection of that part, but which require resection of the entire limb.

(3) Extensive dissecting aneurysms of the femoral artery.

(4) Crushing injuries of the hip region, with gas infection.

(5) Tuberculosis of the femur.

* Presented before the Academy of Surgery of Detroit, Mich., February 13, 1936.

TABLE I

REPORTS OF 15 INTERINNOMINO-ABDOMINAL AMPUTATIONS

1935–1941

Surgeon	Date	Sex	Age	Disease	Result	Published
Gersh	1936	M.	60	Sarcoma	Died after three months from intercurrent infection	Sovet. Khir., No. 4, 681, 1936
Shvartz	1938	M.	48	Periosteal sarcoma	Died within one month from peritonitis and pulmonary infection	Vestnik Khir., **55**, 51, Jan., 1938
Banet	1936	M.	27	Osteosarcoma	Alive at least one month after operation	Bol. Liga Contra il Cancer, **11**, 43, Feb., 1936
Leriche and Stulz	1937	M.	23	Ewing's reticulosarcoma	Alive two months later	Mem. acad. Chir., **64**, 31, Jan. 12, 1938
Padovani	1938	M.	18	Myeloma	Alive six months later	Mém. acad. Chir., **65**, 361, Mar. 8, 1939
Ricard and Clavel	1938	M.	36	Osteosarcoma	Died same day	Lyon Chir., **35**, 81, Jan., 1938
Pascalis	1936	M.	44	Osteosarcoma	Survived operation	Progrès Méd., **39**, 1481, Sept. 26, 1936
Gordon-Taylor	1935	M.	17	Spindle cell sarcoma	Living five years later	Brit. Jour. Surg., **27**, 643, April, 1940
	1936	F.	37	Osteolytic sarcoma	Died three hours after operation	
	?	F.	25	Spindle cell sarcoma	Living three years later	
	1938	M.	14	Osteosarcoma	Died six months later from metastases to spine	
	1938	M.	34	Spindle cell sarcoma	Died 20 hours after operation from shock	
	1939	M.	26	Chondrosarcoma	Survived operation	
Rapant	1937	M.	29	Osteolytic sarcoma	Survived operation	Chirurg., **10**, 804, Nov. 15, 1938
	1937	M.	14	Osteolytic sarcoma	Survived operation	

Certain rules are accepted in selecting this operation. If, after complete physical examination, a malignant tumor is found, careful search must be made for local and distant metastases, especially to the lungs and thorax. The disease should not have penetrated into the pelvis nor beyond the boundaries of the sacro-iliac joint and symphysis pubis. The patient should be a reasonable risk; and should understand that he risks his life in the hope that he will be relieved from the disease or pain he suffers.

Since these rules were first laid down, the recognition of the importance of a transfusion administered during the operation has greatly lowered the mortality, and the patient can approach the operation with greater probability of recovery.

Case Report.—C. B., white, male, age 40, reported to another hospital, December 31, 1934, complaining of a sprain in the right leg, the result of recent heavy lifting. Physical examination revealed an inflamed mass in the right proximal thigh, accompanied by general malaise, chills, and fever. He returned to work after symptoms had subsided, only to be incapacitated a short time later by a recurrence of symptoms. In February, 1935, the mass was aspirated but nothing was obtained; it was removed locally after signs of inflammation had subsided. The patient felt better, gained ten pounds in weight, and returned to work.

He remained symptom-free until August 5, 1935, when he was referred to us because of a large, stony-hard, nonfluctuant mass in the anterior right thigh, and a loss of 30

pounds in weight. A specimen was taken for biopsy under light general anesthesia. The tumor was 5 cm. in diameter, partly fibrous in appearance, nonencapsulated, with necrotic center and some blood. Microscopic examination revealed extensive necrosis with small islets of spindle cell sarcoma surrounding the blood vessels. The pathologist believed that the tumor had not metastasized, and if completely excised would probably not recur. He was hospitalized for further observation with this end in view.

FIG. 1.—The medial aspect of the resected right lower extremity, showing tumor.

Roentgenologic examination revealed a marked soft-tissue swelling of the right thigh; there was no evidence of involvement of the bony structure except a slight pressure deformity in the shaft of the femur below the lesser trochanter. *Laboratory Data:* Negative Kahn; negative urine, no Bence-Jones bodies; R. B. C. 2,880,000, with 40 per cent hemoglobin; W. B. C. 17,000, with 91 per cent polymorphonuclears and 7 per cent lymphocytes. His blood was Type II, and donors were readily found among the family.

With the object of preparing the patient for an interinnomino-abdominal amputation, he was given preliminary roentgenotherapy,* divided into three doses; one on September 25, another on September 26, and a third on September 27, and, in addition, he was given 350 cc. of whole blood on the first day and 400 cc. on the second.

* The deep therapy consisted of the following dosage:

August 25, 1935—Right thigh, Machlett 1, Cone 2, 200 KV, 1.5 Mm. cu., 1 Mm. al., 50 cm. std., 20 ma., 30 min., 600 ma., 100 per cent S.U.D.

August 26, 1935—Right inguinal region, ant., same technic, 55 cm. std.

August 27, 1935—Outer aspect upper third right thigh, same technic.

Following the roentgenotherapy the patient was very weak and slightly delirious, but after the biopsy incision, which permitted drainage of the straw-colored contents, the toxemia lessened, he gained strength, became rational, and on September 30, 1935, the interinnomino-abdominal amputation was performed.

Operative Procedure.—Under spinal anesthesia, the patient was turned a little to the left side by means of sand bags, and, with careful attention to hemostasis, the incision

FIG. 2.—The lateral aspect of the resected right lower extremity.

was made along the iliac crest, down through the inguinal region well above the site of the tumor, and carried to the inner side of the thigh to form a large posterior flap. The upper edges of the wound were then dissected onto the lower abdominal wall, the inguinal canal exposed, the external ring divided, and incision made medially to divide the attachment of the rectus muscle. The external oblique fascia was separated parallel with the inguinal canal as far as the anterior iliac spine; the muscles of the abdominal wall were divided at their insertion on the iliac crest, and the incision carried backward to the posterior superior iliac spine. The internal oblique was pushed up from Poupart's ligament exposing the external iliac vessels. The external iliac artery and vein were encircled separately by a heavy silk ligature and held by clamps, so that in case it became necessary to terminate the proceedings before completion of the operation, the blood supply to the lower extremity could be resumed.

The incision was next carried down on the posterior inferior iliac spine, well away from the genital crease, down the thigh, posteriorly-and-around, to connect with the anterior incision, thus forming a large flap on the inner side. The gluteal muscles were partially divided, and the tissues freed from the greater sciatic foramen. The inferior gluteal artery was ligated, the psoas muscles divided, and the posterior portion of the ilium exposed.

The ilium was divided just lateral to the sacro-iliac joint, the division extending toward the greater sciatic foramen; a forceps was placed in the foramen, a Gigli saw was drawn through, and another forceps inserted from above—beneath the muscles covering the inner surface of the ilium—to grasp the saw and bring it up to the superior border. The bone was then divided completely with the saw.

After the ilium was divided and drawn outward, the sacral plexus was exposed; then the nerve trunks were injected with 2 per cent novocain, all nerves cut, but the iliac vessels were not exposed. The abdominal contents, covered by peritoneum, were freed from the soft tissues covering the ilium, and held mesially by manual retraction. The symphysis and adherent tissues posterior thereto were divided more completely, the spermatic cord being held well out of the way to avoid injury. The right side of the pelvic ring and the lower extremity were removed, the vessels ligated, and the flaps sutured with silk-

FIG. 3.—Roentgenogram of the pelvis after resection of the ilium, ischium and pubis on the right side.

worm gut. Careful approximation of the flaps was not attempted as the blood supply was considered more important. Three cigarette drains were inserted beneath the flaps and dressings applied.

The anesthetic consisted of 15 mg. (0.25 gr.) of novocain and 45 mg. (0.75 gr.) ephedrine dissolved in spinal fluid. It was administered at 11:57 A.M.; the first incision was made at 12:05 P.M.; at 1 P.M. nitrous oxide and oxygen were added and transfusion begun. The operation ended at 1:30 P.M. Pulse and blood pressure were normal throughout. The patient was returned to the ward in good condition, warm blankets were applied, and a second transfusion administered later in the day.

Subsequent Course.—From Figures 3, 4 and 5 it will be seen that an uneventful recovery ensued. The edges of the flap sloughed away, producing a clean granulating surface, which was covered by epithelium in a few weeks. The patient was discharged December 19, 1935.

Two months after discharge from the hospital the patient was placed in the hands of a prosthesis maker to solve the problem of providing support in the absence of one-half of the pelvis. There had been a gain in weight and an absence of pain. On March 2, 1936, a small nodule appeared in the skin flap and microscopic examination showed this to be spindle cell sarcoma.

This return of a sarcomatous growth in the skin flap, even though the sarcoma has been widely excised, is quite common, and such recurrences have been frequently reported.

On March 10, 1936, the patient was readmitted to the hospital for roentgenotherapy and, on March 26, 1936, generalized convulsions lasting a few minutes developed, followed by difficulty in speech and motor involvement of the right upper extremity. The con-

vulsions continued and the patient died, April 2, 1936. The cause of death being due to spindle cell sarcoma with intracranial metastases.

FIG. 4.—Posterior view of patient, with completely healed hind quarter resection.

FIG. 5.—Front view of patient, with completely healed hind quarter resection.

SUMMARY

A brief review of Taylor and Wiles'[1, 2] survey, with a review of the current literature on reports of interinnomino-abdominal amputation since 1935, has been presented.

The case of a white male, age 40, with a spindle cell sarcoma of the right thigh is reported. A description of the procedure for a complete hind quarter resection is given. The importance of careful preparation for operation, and the administering of a transfusion during the operation is emphasized.

The patient recovered from the operation but died six month later of intracranial metastases.

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AN OPERATIVE TREATMENT FOR RECURRENT DISLOCATION OF THE SHOULDER

STEPHEN WAHL, M.D.

NEW YORK, N. Y.

FROM THE SERVICE OF DR. LEO MAYER, HOSPITAL FOR JOINT DISEASES, NEW YORK, N. Y.

A REVIEW of the literature on the operative treatment of recurrent dislocation of the shoulder reveals that there is practically no other orthopedic condition for which so many differing operative procedures have been devised. This, in itself, indicates a lack of unanimity of opinion as to the value of these procedures. This is in part due to the lack of opportunity for intensive numerical experience because of the relative infrequency of this condition. One thing is evident from this review, that the simplest procedures are the most popular.

The operative technics usually employed fall into two major groups: (1) Those which aim to repair the cause of the recurrent dislocation of the shoulder; and (2) those which attempt to prevent the recurrence of the dislocation regardless of the causative factor. It is not the purpose of this presentation to review all of the operative methods devised for this disturbance. I shall merely restrict myself to those groups of procedures which utilize the long head of the biceps tendon as a suspension apparatus for the head of the humerus in order to prevent the recurrence of the displacement.

The advantages of the use of the long head of the biceps are: (1) It makes possible the construction of an arrangement similar to a strong ligamentum teres in the hip; (2) it is available at the site of the operative procedure; and (3) it eliminates the necessity for additional incisions to obtain fascial or tendon transplants.

In 1926, Rupp[1] expressed the belief that the long head of the biceps was the causative factor in the recurrence of the dislocations because of pressure on the head of the humerus in downward and outward directions on certain motions of the arm. He, therefore, unwittingly made a suspensory apparatus out of the long head by suturing it to the capsule and periosteum of the humerus. The results of this procedure were not very satisfactory because, in all probability, a firm tendo-osseous union was not obtained in most of his cases.

Heymanowitsch,[2] in 1927, described two variants of a suspension procedure. In the first variant, he freed the whole biceps tendon and severed its origin at the upper rim of the glenoid. He then drilled a hole through the head of the humerus and threaded the freed tendon through this bone channel and fixed the proximal end to the acromion. In the second variant, he cut the tendon at the level of the surgical neck of the humerus, drilled a channel as previously, through the head of the humerus, threaded the proximal portion of the severed tendon through the channel, and reunited the cut ends of the biceps tendon.

In 1929, Nicola[3] described an operation, independently of Heymanowitsch, which is identical with the latter's second variant. Nicola's description popularized this method in this country.

In 1933, Roberts[4] described an operation in which the long head of the biceps was buried in a deepened bicipital groove. Burnets[5] achieved remarkably good results with this method.

The Heymanowitsch-Nicola procedure, though relatively simple, presents certain practical objections and technical difficulties. This procedure neces-

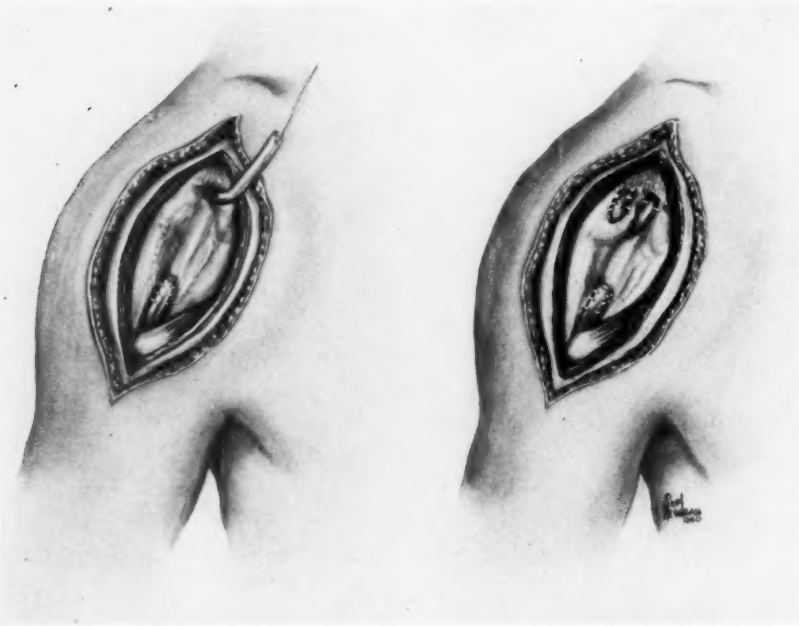

FIG. 1.—Showing the proximal part of the cut tendon of the long head of the biceps lifted out of the bicipital groove. The distal end is fixed to the periosteum.

FIG. 2.—Showing the proximal part of the cut tendon pulled through the bone channel in the greater tuberosity of the humerus, and fixed snugly to the surrounding tissue.

sitates the opening of the scapulohumeral joint, thus exposing it to unnecessary trauma and involvement in the event of an untoward infection with the possible dire after-effects. Technically, the drilling of the channel and the threading of the tendon through the channel may at times be difficult, necessitating considerable manipulation and trauma to the joint cartilage as well as to the tendon, and prolonging the operation. Furthermore, improper placement of the channel may result in recurrences. To overcome these objections I[6, 7] have described, in 1931, a simpler, safer and more certain procedure (Figs. 1 and 2).

Operative Technic.—This consists of a three-inch long, longitudinal skin incision starting just below the medial border of the acromion and overlying the bicipital groove. The deltoid muscle is split longitudinally by blunt

dissection and if the groove does not present itself in the operative field it can be brought into view by rotating the arm internally or externally. The sheath of the long head of the biceps is incised and the tendon is freed from the sulcus. About one inch above the muscular portion of the long head of the biceps, strong silk sutures are placed fixing the tendon to the periosteum while the forearm is held in 45° flexion. A stay suture is placed immediately above the fixation sutures. The tendon is cut below the stay suture and is lifted out of the bicipital groove. A drill hole measuring about one-half to three-quarters of an inch in length is made extending from the bicipital groove through the greater tuberosity. The free end of the cut tendon is then scarified and threaded through this channel while the arm is held in 45° abduction. The tendon is snugly fixed to the periosteum and the surrounding tissues with strong silk sutures. The wound is then closed and the extremity is immobilized in a plaster of paris spica in 45° abduction or in a Velpeau bandage for a period of three weeks. On removal of the bandage the patient usually presents a complete range of motion. Several weeks of physiotherapy complete the after-care.

In addition to my[6] four cases, published in 1931, I have employed this procedure on ten other patients, making a total of 14 cases. Of these, 11 were males and three were females. Nine were laborers, and the others had less strenuous occupations. One of the laborers was an epileptic. Twelve of these patients were under my personal observation for three to six years, one for one year and nine months, and another for one year. All of these had had frequent dislocations of many years' standing, at times on the slightest motion of the arm or the slightest exertion such as sneezing or coughing. The above mentioned epileptic sustained, during a seizure, a fracture of the olecranon of the same extremity 11 months subsequent to the operative procedure without redislocating his shoulder. Another of these patients had had a previous partial excision and reefing of the capsule, with subsequent recurrence of the dislocation. All of these patients regained a full range of painless motion subsequent to my operative procedure; and all of them returned to their previous occupations without any disability whatsoever. None have had a recurrence.

Anschütz,[8] Heyn,[9] and Jungling[10] have employed this procedure in six instances. These were followed over a period of six months to over two years. Only one of these reported cases had a recurrence, which occurred at the end of the second year, under circumstances which were not disclosed.

Eleven other cases are known through personal communications with three surgeons[11, 12, 13] who observed them for a period of over two years. None of these patients sustained a recurrence.

Altogther, 31 cases, known to me, have had the above described procedure for recurrent dislocation of the shoulder. Twenty-eight of these have been observed for two to six years. Only one of them has suffered a recurrence of the dislocation.

SUMMARY

(1) This communication describes additional experience with a simple, safe and effective operative procedure for recurrent dislocation of the shoulder.

(2) Thirty-one known cases have been followed by the author and other surgeons, with only one recurrence.

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SUBTALAR DISLOCATIONS

CASE REPORT OF THE INWARD TYPE

ROBERT A. WISE, M.D.

NEW YORK, N. Y.

FROM THE SURGICAL SERVICE OF KNICKERBOCKER HOSPITAL, NEW YORK, N. Y.

WITH the intense interest shown during recent years in the treatment of fractures, it is surprising that the study of dislocations has been neglected. Some of these injuries may test to the utmost the anatomic knowledge and ingenuity of the surgeon if they are to be clearly understood and successfully treated. This is particularly true of subtalar dislocations of the foot; for, when such a condition is encountered, even after careful study of the roentgenograms, it is often difficult to understand its true nature and to institute proper treatment.

A subtalar dislocation is a rare traumatic injury of the foot in which the calcaneus and navicular are displaced, the talus retaining its normal position within the ankle mortise. The displacement of the foot upon the talus can be inward, outward, backward or forward. Baumgartner and Huguier[2] collected all recorded cases up to 1907, and Shands[26] made an additional collection to 1927.

It is the purpose of this paper to report a case of subtalar dislocation of the *inward* type and to discuss the pathology and treatment of this unusual and interesting injury. The literature has been reviewed and a résumé made of case reports since Shands' collection of 1927.

Case Report.—J. J., Negro, male, age 52, was admitted to Knickerbocker Hospital January 25, 1940. He stated that he slipped while walking on an ice-covered pavement; his right foot turning inward, became caught in a depression in the ice and he fell forward across his fixed foot. When attempting to rise, he felt severe pain in his right ankle and noticed that his foot was fixed in an inverted position.

Physical Examination: The right foot presented an astonishing deformity (Fig. 1); it was markedly inverted, plantar flexed and displaced inward. The inner border of the foot was elevated, the outer border depressed and the plantar surface faced the opposite foot. On the outer side of the foot the lateral malleolus was unusually prominent, and anterior to it was a large immovable bony mass, identified as the head of the talus, over which the skin was tightly drawn, smooth and tense. The body of the talus could be palpated on the dorsum of the foot, in its normal relation to the tibia; and slight active flexion and extension of the foot at the ankle was possible. No active or passive inversion or eversion was possible, the foot being held in its abnormal varus position as in a vise. There was considerable swelling about the foot and ankle but the skin was unbroken.

Roentgenograms (Figs. 2, 3, 4) revealed a subtalar dislocation of the inward type.

Treatment: One hour after the injury, under cyclopropane-oxygen anesthesia, closed reduction was accomplished. *Manipulative Technic:* With the knee flexed in order to relax the tendo Achilles, the foot was grasped with the left hand under the heel and the right hand about the metatarsal region, and while steady traction was applied downward in the axis of the leg, the foot was placed in dorsiflexion and everted, as an assistant exerted pressure on the head of the talus. As reduction took place, there was a sharp report which could easily be heard across the room. A plaster casing was applied from

the toes to the tibial tuberosity, the foot being held at a right angle with the leg and neutral to inversion and eversion. Examination and roentgenograms (Figs. 5, 6, 7) showed that satisfactory reduction had been obtained.

After Care: The casing was removed four weeks after reduction and active motion of the ankle and foot was encouraged. Light weight-bearing was started six weeks, and full weight-bearing seven weeks after the injury. Normal range of subtalar and ankle motion returned rapidly, and ten weeks after the injury, the patient walked without pain or limp, and had returned to work.

FIG. 1.—Before reduction, showing inversion of the foot and prominent head of the talus.

The first reported case of subtalar dislocation was by Hey,[14] in 1810. Before this time the condition was confused with midtarsal, complete talar and ankle dislocations. Cases were reported by Judcy[15] and Dufaurets,[9] in 1811, and by Sir Astley Cooper,[6] in 1815. Nelaton,[20] in 1835, described a dissection of a typical case of the outward type, and, in 1847, gave a detailed description of the injury in his Pathologue Chirurgicale. Wells,[20] Arnott,[1] McDonnel,[17] and Hancock,[13] made early contributions in case reports.

Broca,[4] in 1852, in an outstanding paper, analysed all reported cases, gave the name subastragaloid to the dislocation and described the inward, outward and backward types. He demonstrated that the talus retains its normal relationship in the ankle mortise and that the navicular and calcaneus,

together with the other tarsal bones, are displaced. Malgaigne,[18] in 1855, described the forward type but considered the talus the dislocated bone and, reversing the nomenclature of Broca, classified the types according to the position of the head of the talus. Broca's terminology is universally used to-day, the types of the dislocation being classified according to the position taken by the foot and not that taken by the head of the talus.

Quenu,[22] in 1883, described a dissection of a case of the inward type, analysed the causes of irreducibility and wrote on the treatment of all the types. In 1907, Baumgartner and Huguier,[2] in a remarkable treatise, collected all case reports in the literature, described the mechanism and pathology

FIG. 2.—AP. view of the ankle, showing medial displacement of the foot at the subtalar joint. Note normal relationship of the talus in the tibiofibular mortise.

FIG. 3.—Oblique view of the foot and ankle showing disruption of the talonavicular joint.

FIG. 4.—Ventrodorsal view of the foot showing the head of the talus lying over the calcaneocuboid articulation.

after experimental production of the dislocation and discussed the treatment of the various types. This paper and that of Broca are classics in the literature of the subject. Reismann's[24] report, in 1907, analysed the mechanism of the injury and described in detail the anatomy and physiology of the subtalar joint. Thienhaus,[28] in 1907, Moore,[19] in 1922, and Shands,[26] in 1927, have written excellent papers in English.

Pathology: In typical dislocations of the *inward* type, the head of the talus is completely separated from the navicular and lies at the lateral side of the foot on the superior surface of the cuboid. The extensor tendons are medial to, and the cruciate crural ligament beneath, the head of the talus. The calcaneus is displaced inward. Ligamentous damage is extensive with rupture of the dorsal talonavicular, the interosseous talocalcaneal, the anterior and lateral talocalcaneal and the anterior talofibular ligaments. Rupture of the powerful interosseous talocalcaneal ligament is essential to the production of the dislocation. In the *outward* type, the head of the talus lies on the medial side of the foot in relation to the inner surface of the navicular, while the calcaneus is displaced outward. In the *backward* type, the calcaneus is displaced backward and the head of the talus rests upon the superior surface

of the navicular. In the *forward* type, the calcaneous is displaced forward and the head of the talus rests upon its superior surface.

Compound dislocations with protrusion of the head of the talus occur frequently. Dehoey[7] collected 26 compound dislocations of all types. Necrosis

FIG. 5. FIG. 6.

FIG. 7.

FIG. 5.—After reduction.
FIG. 6.—After reduction, lateral view of the foot and ankle.
FIG. 7.—After reduction, AP. view of the foot showing normal talonavicular articulation.

of the skin tightly stretched over the head of the talus, resulting in a compound wound, occurs as a complication of late reduction. In Larget's[16] casé, skin necrosis developed four hours after the injury.

A careful search of the literature reveals ten cases of subtalar dislocation reported since Shands' collection in 1927. There are seven dislocations of the inward type and three of the outward type; three are compound and two have associated fractures. A short synopsis of these case reports is appended:

REPORT OF TEN CASES OF SUBTALAR DISLOCATION

From the Literature Since 1927

Case 1.[25]—A female, age 40, getting off her bicycle, stepped in a hole in the street. *Examination* showed the left foot to be fixed in inversion. The head of the talus was prominent on the outer border of the foot. Roentgenograms showed a subtalar dislocation of the inward type.

Treatment.—Closed reduction.

Result.—Normal ankle and foot movements.

Case 2.[25]—Male, age 47. While riding a bicycle, the patient was struck and run over by an automobile. *Examination* showed the left foot to be in extreme supination. The skin on the lateral aspect of the dorsum of the foot was tightly stretched over the prominent lateral malleolus and the head of the talus. Roentgenograms showed a subtalar dislocation of the inward type.

Treatment.—Closed reduction.

Result.—Normal foot and ankle movements.

Case 3.[21]—Male, age 39, jumped into a trench. *Examination* revealed the left foot to be fixed in a marked varus position. There was a large, dirty wound on the lateral aspect of the foot through which the head of the talus and the lateral malleolus protruded.

Treatment.—Astragalectomy.

Result.—Excellent functional result, with motion at the new tibiotarsal articulation.

Case 4.[5]—Female, age 72, fell on her inverted right foot into a pit three feet deep. The foot was immobilized in plaster without reduction. One month later roentgenograms showed that reduction had not been made and *examination* revealed the foot to be fixed in marked supination and plantar flexion. The head of the talus was prominent on the outer border of the foot. Roentgenograms showed a subtalar dislocation of the inward type.

Treatment.—Closed reduction with the aid of an Esmarch bandage.

Result.—Normal foot and ankle motions.

Case 5.[10]—Male, age 35, while pushing on the foot brake of his car, crashed into the rear of a truck. *Examination* showed the foot to be in marked inversion with slight plantar flexion. There was a prominence in the region of the lateral malleolus. Roentgenograms revealed a subtalar dislocation of the inward type with a fracture of the body of the talus.

Treatment.—Closed reduction.

Result.—Complete return of joint function.

Case 6.[25]—Male, age 53, slipped from a stepladder and fell to the floor. *Examination* showed the typical findings of a subtalar dislocation of the inward type.

Treatment.—Closed reduction.

Result.—Normal motions of the foot and ankle.

Case 7.[3]—Male, age 39, slipped off a chair falling on his left ankle. *Examination:* The left foot was fixed in an equinovarus position. The lateral malleolus was prominent almost piercing the skin and the head of the talus presented at the outer aspect of the foot. Roentgenograms revealed a subtalar dislocation of the inward type.

Treatment.—Closed reduction.

Result.—Complete return of joint function.

Case 8.[23]—Female, age 20. The patient fell six feet from a trapeze, landing on her right foot. *Examination* revealed the right foot to be in an exaggerated pronated position. The head of the talus protruded through a wound on the inner side of the foot, below and anterior to the medial malleolus. The tendon of the tibialis posterior was seen in the wound, lying on the superior surface of the head of the talus preventing reduction.

Treatment.—Débridement and open reduction.

Result.—There was complete loss of subtalar motion, but ankle motion was within normal range.

Case 9.[12]—Female, age 62, tripped on the metal guard of a street car step and her left foot came down forcibly on the step below in a pronated position. She noted that her foot was turned markedly outward. Roentgenograms revealed a subtalar dislocation of the outward type with associated fractures of the cuboid and lateral malleolus.

Treatment.—Closed reduction.

Result.—There was 50 per cent limitation of inversion and eversion of the foot.

Case 10.[11]—Male, young, received a blow on the outer surface of his right foot at the level of the lateral malleolus. *Examination* showed a large wound on the inner side of the foot, extending from the medial malleolus backward to the tendo Achilles. The foot was rotated so that its plantar surface presented outward, with its inner border depressed. The talus retained its normal relationship with the ankle mortise.

Treatment.—Débridement and open reduction.

Result.—Normal ankle motion. There was considerable limitation of inversion and eversion of the foot.

Treatment: In simple, early cases, closed reduction is usually readily accomplished by traction and manipulation—the method of reduction depending upon the type of dislocation under treatment. General or spinal anesthesia is necessary, and the knee should be flexed in order to relax the calf muscles.

Inward Type: Reduction is obtained by traction downward in the axis of the leg and the foot is dorsiflexed. As pressure is exerted on the head

of the talus, the foot is everted. If sufficient traction cannot be obtained by grasping the foot, a Kirschner wire through the calcaneus will make a more powerful pull possible.

Outward Type: Reduction is performed by similar downward traction, the foot being inverted as pressure is exerted on the head of the talus. Cases of this type, in which reduction is prevented by the tendon of the tibialis posterior may be successfully reduced, at times, if the foot is forcibly dorsiflexed in order to relax this tendon.

Backward Type: Reduction of dislocations of this type is accomplished by the method described by Destot.[8] The foot is forced into extreme plantar flexion and, as forward traction is placed on the calcaneus, the head of the talus is pressed into its normal relationship with the navicular.

Forward Type: Broca's[4] case is the only one in the literature in which closed reduction was successful. He applied downward traction on the foot to disengage the calcaneus from beneath the talus and then pulled the foot backward. Cases of this type reported by Thienhaus[28] and Smith[27] were old and both required open reduction.

Arthrotomy is indicated when closed reduction is unsuccessful. The incision is made directly over the prominent talar head and the cause of the irreducibility is removed. The cruciate crural ligament, drawn tightly about the head of the talus, is the most frequent cause of unsuccessful reduction in dislocations of the inward type. The tendon of the tibialis posterior, lying upon the neck of the talus and between it and the navicular, frequently makes reduction impossible in dislocations of the outward type. Division of this tendon may be necessary.

Late, unreduced cases, in which treatment has been delayed and degeneration of the articular cartilage has developed, are best treated by talocalcaneal and talonavicular arthrodesis after open reduction, as suggested by Wilson.[30] However, Clavel's[5] case (Case 4), which was unreduced for four weeks, demonstrates that a good result may be obtained in a late case by simple, closed reduction.

Compound subtalar dislocations were formerly treated by excision of the talus. With the development of better methods of handling compound wounds, these injuries can now be safely treated by careful débridement, reduction and immobilization. Excision of the talus should be reserved for late, infected cases, and for those associated with a badly comminuted fracture of the talus.

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THE THIRD PHASE OF SURGERY

TOTAL STERILIZATION AS A BASIS OF INTEGRAL ASEPSIS AND OF PASTEURIAN CICATRIZATION

MAURICIO GUDIN, M.D.

MEMBER OF THE FLUMINENSE FACULTY OF MEDICINE, THE SURGICAL ACADEMY OF FRANCE, THE INSTITUTE OSWALDO CRUZ, AND THE NATIONAL ACADEMY OF MEDICINE OF BRAZIL

RIO DE JANEIRO, BRAZIL

THE THREE PHASES

THE fact which strikingly dominates the evolutionary history of surgery is that of the battle of the surgeons against the infection of surgical wounds.

With respect to the fundamental phenomenon of the healing of the operative wound, this battle can be clearly divided into three periods.

The first phase, which has lasted for centuries, is characterized by the ignorance of the existence of microbes.

This was the period of "healing by secondary intention": the systematic suppuration of the wound, with its terrible consequences—septicemia, pyemia, gas gangrene, tetanus, *etc.*

The second phase makes its appearance with the first notions of the existence of bacteria; it is characterized by the possibility which the surgeons have had to control partially, by means of the methods of Lister and of Terrier, the action of bacteria on the operative wound. It is further characterized by the appearance of "healing by primary intention," in direct relation with surgical results which are extraordinary in comparison with those of the preceding period.

Without looking more closely at the reverse of the medal, and despite the statement of Pasteur in 1865: "I shall have to fear only the germs of the air, suspended around the patient's bed," one errs in believing in healing by primary intention on the basis that the wounds eventually may show no contamination.

Nevertheless, to such an extent was this belief held, that when, in July, 1935, I stated before the Surgical Academy of France: "We knew healing by primary intention only under its septic aspect, necessarily followed by an inflammatory reaction," although representing the truth, the Academy considered this to be heresy, and stated in order to safeguard its responsibility: "The office wishes to point out that the authors fully retain the responsibility for their writings."

Everyone should nevertheless know that healing by primary intention takes place, as I have already remarked, in the mouth, the nose; the intestine, the anus, *etc., i.e.,* in a septic medium. The constant contamination of the operative wound which heals by primary intention is an incontrovertible fact. One always operates with instruments and material which are contaminated after having been carefully sterilized in the autoclave. To demonstrate this fact, one has only to cover the surgical equipment with agar and expose it

to the air in an operating room. After incubation, numerous bacterial colonies are found to be present (Fig. 1).

However, it is hardly necessary to go out of one's way to this extent, since we all know that chasing flies in the operating room is part and parcel of the so-called aseptic operative procedure, a fact to which I believe I first

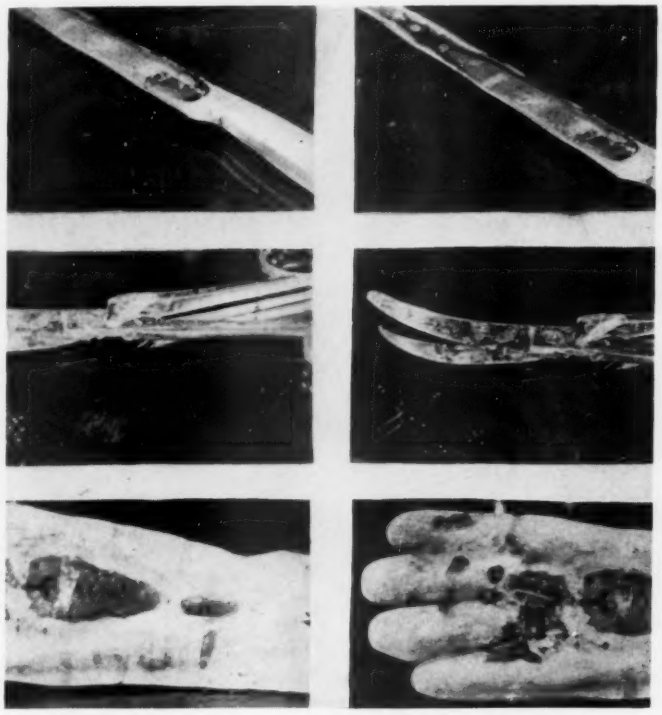

FIG. 1.—Bacterial colonies growing on surgical equipment which was sterilized by autoclave, covered with agar, and exposed to the air in an operating room.

called attention in a paper entitled "Aseptic Method and Fly-Tennis" but, as I discovered later, it had already been commented on by others.

The inflammatory reaction of the wound is visible to the naked eye through redness, edema, and the existence of bacteria in the seropurulent droplets situated where the sutures enter and leave. This contamination is easy to demonstrate bacteriologically and by means of sections which reveal the existence of bacteria in the depths of the tissues.

Furthermore, when the operative wound is reopened during the course of cicatrization—and we are referring now to wounds which are healing by primary intention—one observes a purulent appearance of the healing tissue.

Healing by primary intention is in reality a state of unstable equilibrium which is the consequence of phenomena of infection. On the one hand, we have the contamination of the operative wound (quantity, character, and

degree of virulence of the bacteria), and on the other hand, the defensive reaction of the organism (general and local immunity).

At the present time, these facts completely escape our attention.

Because of these facts, healing by primary intention evolves, unpredictably, either in the direction of its completion or in the direction of suppuration, *i.e.*, secondary intention, or more serious complications.

Healing by primary intention must, therefore, be regarded as the healing of a contaminated wound, the closure of which takes place by direct juxta-

FIG. 2.—This cut is reproduced from the book *Intracranial Tumors*. By Professor Bailey, of Chicago. One sees a nurse hunting flies during the operation! The cut antedates (1933) the one which I published in 1936 in my paper *Aseptic Method and Fly-Tennis*.

position, and which is in general characterized by: (1) An inflammatory reaction; (2) the fact that hematomata suppurate readily; (3) a marked lack of tolerance for foreign bodies which remain in the organism; (4) the more or less frequent necessity of drainage, *i.e.*, of an evacuating agent which is at the same time a contaminating agent.

In practice, it is important to know the result of this permanent and inevitable state of contamination of the operative wound by an aseptic method associated with the presence of bacteria, a method which contains a fundamental source of error.

It is quite obvious that a postoperative period based on this state of unstable equilibrium requires constant vigilance, because of the possibility of accidents.

I believe I am justified in stating that 90 per cent of what is called the postoperative illness is merely due to infection.

In a summarizing review presented before the Surgical Academy of

France on the tenth of July, 1935, and based on the recent statistics of surgeons in all countries whose quality and capacity are beyond doubt, I have called attention for the first time to the long and impressive series of operative accidents and incidents based on the fundamental fact of the permanent contamination of the operative wound. I have reinvestigated all the sources of contamination—the patient's skin, the surgical equipment, the atmospheric air—and I have shown that, in the present state of surgery, it is the contamination of the air to which must be attributed the great majority of these accidents. These accidents run the gamut from a simple extrusion of sutures to the death of the patient.

We have to deal with suppuration, eventration, and evisceration as a result of the rupture of the body wall, with failures in the cure of eventrations, with peritonitis; with osteomyelitis and arthritis in bone surgery; with empyema in thoracic surgery; with meningitis in neurosurgery; with contamination of the cerebrospinal fluid as a result of spinal anesthesia, and with the contamination of tissues in local anesthesia, as well as with septicemia, gas gangrene, cases of tetanus, *etc.*, all this considered, as much as possible, without other factors of contamination (*loc. cit.*).

This list is worth consulting, for, although condensed here, it occupies about ten pages.

It represents the definitive and incontrovertible demonstration of the failure of the usual method, which was originally created in France by Terrier and which has been designated as aseptic, and we are thus made to realize to what extent an operation, under these circumstances, is a test of the power of the organism to resist infection, and how much it is to be desired not to submit the patient to this test.

Leriche, who has seen me operate and who has himself operated by my method at Rio de Janeiro, has appropriately said: "I have weighed all the theoretical objections which one can possibly raise against Gudin's method: difficulty, inconvenience, uselessness, expense. Not one of these is valid. We must not forget that in Lister's time, also, one did not believe that it was necessary to change anything in the traditional practice of surgery. All was well, because it was being done. How many terrible failures there were, nevertheless! And, more recently, have we not seen many surgeons declare themselves against the use of masks and gloves? Man, even if he is a surgeon, is an animal who succumbs to habit formation."

The third phase is total sterilization, the only procedure permitting integral asepsis, which has allowed me to demonstrate a type of healing previously unknown—Pasteurian cicatrization, which profoundly modifies the operative results and is the basis of the third phase of surgery.

THE EXOGENOUS FACTORS OF OPERATIVE CONTAMINATION

These elements are: the patient's skin, the surgeon's hands, the patient's and surgeon's perspiration, the operative equipment, and the air.

The Skin of the Patient.—The disinfection of the skin with tincture of iodine, which had been employed empirically for a long time, was studied

scientifically by Walther in 1909 (Bull. et Mém. de la Soc. Nat. de Chir.; Congrès Inter. de Chir. de Paris, 1910), by means of histologic sections which were impregnated with silver nitrate and which, through the formation of the iodide, made possible the observation that the iodine penetrates the entire thickness of the epidermis and the superficial layers of the dermis, the sebaceous and sweat glands, and the periphery of the hair follicles.

However, when the time came to demonstrate by means of inoculations, that living bacteria were no longer present, the contamination of the air,

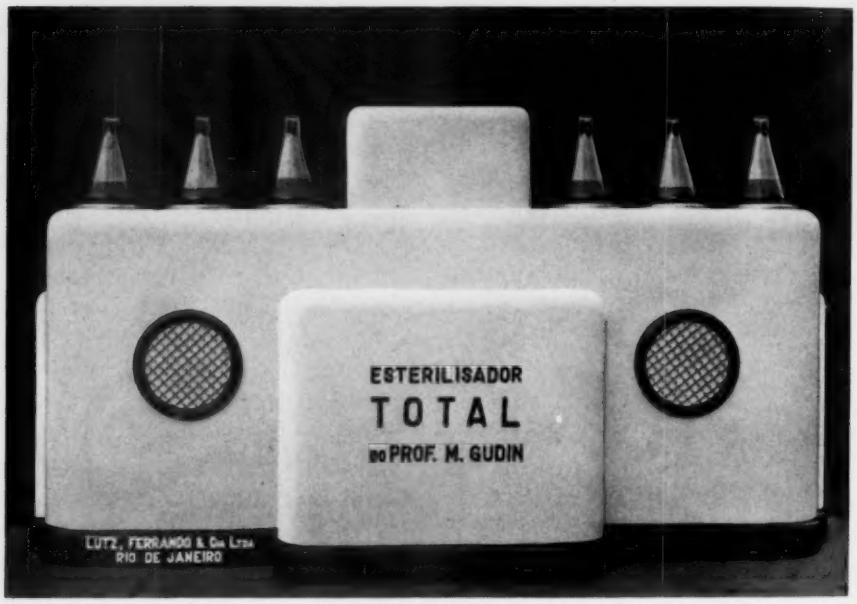

FIG. 3.—The Total Sterilizer. One hour suffices for the sterilization of all the material required for several operations.

inevitable with the ordinary bacteriologic methods, has vitiated the results, thus leaving room for doubt.

The reason is that these experiments, like many others, are above the possibilities of present-day bacteriology; whether it is a matter of sampling of material for culture, or of inoculation, transfer, or tissue culture, or of any other bacteriologic technic, contamination by the air has always remained the stumbling block in bacteriology, an insurmountable one when certain demonstrations are attempted, for it has never been possible to work freely, in sterile air.

The problem of the sterilization of the skin had not been solved, therefore, but has remained of the greatest surgical importance, and attempts had to be made to find an answer.

This is why I have again undertaken these experiments, this time under the protection from contamination by air, and they have enabled me to arrive at the following conclusion: The normal, healthy, accessible skin (the umbilicus is inaccessible, without anesthesia), without callosities, carefully

freed of fat by means of benzine, and treated for at least ten minutes with a freshly prepared 10 per cent solution of iodine, is and remains perfectly sterile.

While one must be very careful to completely remove the tincture of iodine for culture experiments, it is quite unnecessary to do this for surgical operations if freshly prepared tincture is used.

The Hands.—The practical solution which alone permits to keep the skin of the hands in perfect condition consists, first of all, in avoiding their contamination, and subsequently in scrubbing them very carefully for at least ten minutes with hot water and sterile soap, without an antiseptic.

In prolonging this procedure for more than a half hour, one can achieve a real sterilization of the hands, as has been shown by Delbet and Ravaut in 1904 (Bull. Soc. Nat. de Chir.).

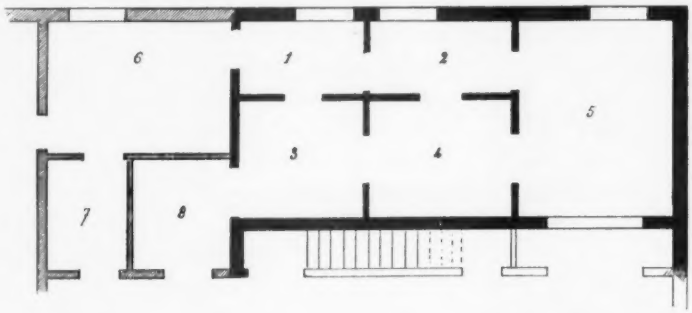

FIG. 4.—Plan of the lower floor of the operating unit, with sterile air-tight compartments of the two-floor operating room. 1 and 2—Surgeon's entrance. 3 and 4—Patient's entrance. 5—Operating room. 6—Professor's room. 7—Assistants' room. 8—Room where the patient is undressed. The portion which is indicated in black is that which is sterilized.

They demonstrated at this time that the hands remained sterile when prepared in this manner and were covered by gloves, but that the latter were not sterile, because of their exposure to the air! But the hands do not resist a daily treatment of this sort. In practice, as far as dressing and putting on gloves are concerned, one must proceed as if the hands were septic.

Sweating.—No asepsis is possible if the patient or the surgeon perspires. In this connection, the use of conditioned air is imperative.

The Operative Equipment.—The sterilization of water, instruments, gloves, sponges, sutures, carried out according to a rigorous technic, taken by itself, leaves nothing to be desired.

As far as catgut is concerned, this material is the source of numerous operative annoyances, as has already been pointed out by Kauffmann and Galéa who studied the causes of postoperative tetanus (Jour. de Chir., February, 1932). This source must be sought elsewhere. Always sterile if it is transferred from sealed tubes into the culture broth in sterile air, as I have had occasion to observe in numerous trials, it produces cultures as soon as it is exposed to the air, just as any other surgical equipment. It cannot be

doubted that by virtue of being wet it attracts a much larger number of bacteria than silk or linen threads, which are dry.

As regards the question of postoperative tetanus in connection with operations without endogenous septic focus, the only surprising thing is the rarity of its occurrence, which must evidently be attributed to the fastidious requirements of an anaerobic organism like the bacillus of Nicolaier. The presence of tetanus bacilli in operating rooms is frequent. It is easy to see with what impunity operating rooms are soiled by dirt carried in on the shoes of assistants. It is not from the point of view of contamination that I consider catgut as an undesirable thread, while operating in a sterile medium, but because it is resorbable and therefore lacks solidity. Therefore I use it only exceptionally, namely, in septic cases or when other sutures would run the risk of undergoing a process of incrustation.

FIG. 5.—The surgeon, completely protected by the sterile suit.

The Air in the Operating Rooms.—The air is the source of contamination which it has not been possible to control. The construction of operating rooms with material which is easily washable, with rounded corners and a few other provisions, contribute very little to the battle against an element which is so subtle and mobile, and which surrounds us everywhere.

It consequently represents a permanent factor of contamination of the operative wound, unless it is sterile.

It acts: (1) Through the bacteria which are suspended in the room air; (2) by the displacement of those which are deposited everywhere; (3) by the carriage of bacteria into the room by all persons, vehicles, and material coming from the outside; (4) as a carrier of bacteria from the respiratory pathways and mouth of those who talk, sneeze, and cough, even when they are protected by a mask; (5) under the influence of conditions of temperature, of currents, of the presence of water, which one finds in the form of vapor, drops of Flügge, microscopic droplets of Trillat (of the Institut Pasteur), which, because less than one micron in diameter, escape almost entirely the action of gravity, while containing "alimentary gases" which sustain life and reproduction of organisms. The latter are easily transported along great distances and without difficulty penetrate the pulmonary alveoli, in spite of the defensive apparatus of the respiratory tract, which is normally effective against bacteria which present themselves under different conditions (Trillat, C. R. de l'Acad. des Sci.: Sur les Conditions de Transport des Microbes de l'Air, 1913; Influence de l'Humidité, 1920; Activité de l'In-

fection par les Voies Aériennes, 1921 and 1925; Influence des Agents Extérieurs sur la Contagion, Rev. d'Hygiène, June, 1932).

About 30 or more years ago, Miquel, Müller, Flügge, Lafolie, Fournier, Sartory, and Tuffier studied the bacteria in operating rooms, more recent

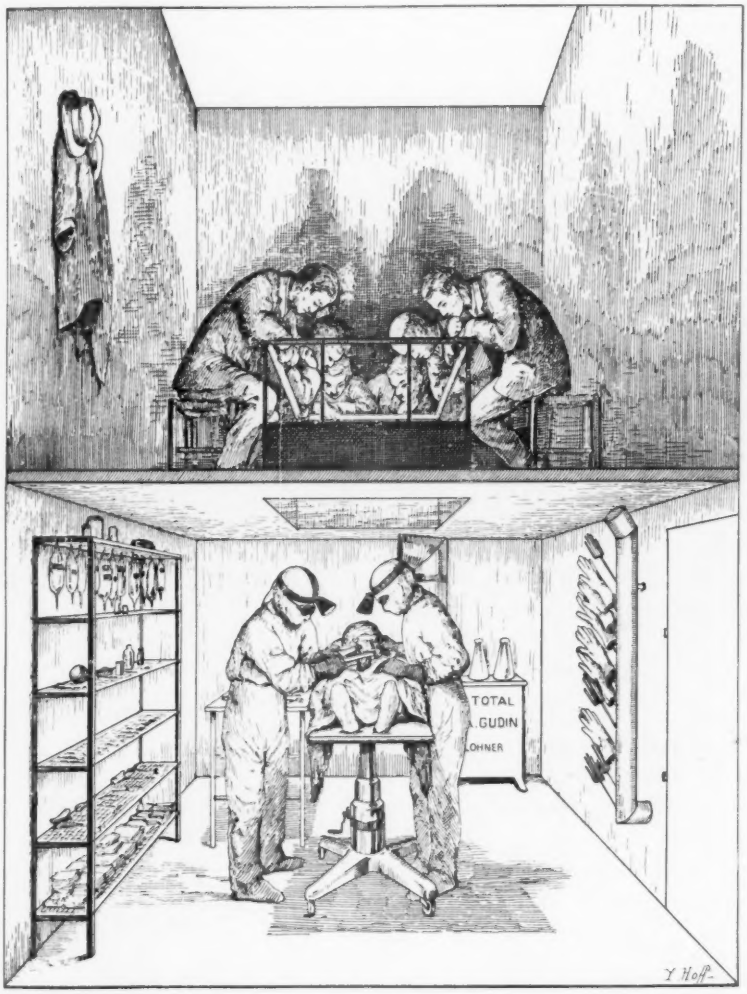

FIG. 6.—The operating room is very low; a very close view is obtainable, directly down upon the operative field, which fact enables one to see the operative details, so that the students really spend their time profitably.

work has merely confirmed the data contributed by them. It was shown that the predominating pathogen is the staphylococcus, and others which were found are the streptococci, the colon bacillus, the pneumococcus, the tubercle bacillus, the tetanus bacillus, as well as other anaerobes, according to circumstances (Kole and Wassermann).

The most important work on this subject, however, which has since been confirmed by numerous authors, was that of Quému and Landel (1902) who, after two years of much laborious research, published an important memoir in Bull. et Mém. de la Soc. de Chir. de Paris, under the title Micro-organismes de l'Air dans les Salles d'Opérations. Recherche d'un Procédé de Désinfection.

They have shown: (1) That agar plates of a surface of 65 cm.^{2}, exposed for an average duration of ten minutes, give an average of 80 colonies per plate; (2) that this number is tripled or quadrupled as soon as assistants, wearing sterilized gowns, enter the room; (3) that when a certain quantity of dust collected in the room is injected into guinea-pigs, abscesses, phlegmons, and septicemia are produced, in confirmation of the older experiments of Miquel, one of Pasteur's students, who during a period of 30 years had studied the problem of the atmospheric bacteria so well that very little has since then been added.

Flügge, using *Micrococcus ferruginosus*, has shown that even when one speaks with a low voice, without a mask, one contaminates agar plates at a distance of several meters.

Numerous investigators have demonstrated with sufficient probability (considering that these experiments have a character of precision only in a sterile atmosphere) that even while wearing a mask the surgeon who talks contaminates plates at a distance.

I have observed—and this observation is possible only in a sterile atmosphere—that the surgeon whose face is well covered and who breathes normally does not contaminate the atmosphere if he does not talk.

The question of the contamination of the mask is a delicate one. The mask is always forcibly contaminated—first of all by the skin of the face if one forgets to sterilize it (as I have seen happen in the experiments which I know of), and, secondly, by contact with the mouth and the external nares, which regions cannot be sterilized.

The local contamination of the mask is not necessarily followed by that of the atmosphere.

The problem of the contamination of the air has been based on the conception of Lister who, at a time when the pyogenic bacteria were still unknown, was able to point out the analogies between the phenomena of infection and those of fermentation, which latter Pasteur had just demonstrated (1864).

Since the contamination of the air may be the result of various factors, and since further study results only in confusion the great majority of surgeons finally believed very little or not at all in atmospheric contamination.

The statement made by Kauffmann and Galléa (*loc. cit.*): "Present-day sterilization and the use of gloves makes impossible the transfer of germs from the hands or the instruments of the surgeons," corresponds to the general conviction which, as I showed already in 1930 (Gudin: Presse Méd., April 16, 1940—Méthode Opératoire Stérile), but is quite erroneous.

THE REASON FOR THE FAILURE OF THE ATTEMPTS MADE TO STERILIZE THE AIR OF OPERATING ROOMS

It is impossible to introduce a sterile substance into a container contaminated by bacteria without contamination of the substance.

It is just as impossible to sterilize any substance in a container if the process of sterilization does not succeed in sterilizing container and content simultaneously.

The disregard of these two fundamental bacteriologic facts is the reason for the failure of all attempts made to sterilize the air in operating rooms.

In all these attempts one has never thought of using the means necessary for avoiding the contamination of the room, as Leriche has appropriately pointed out in his communication to the Royal College of Surgeons of London (April 5, 1939).

It is, therefore, useless to analyze and discuss in detail the numerous processes, all of which are vitiated by this fundamental error, such as filtration through various substances (Bellanger, Trenel, *etc.*); the passage of the air through metallic gauze heated by electricity (Sartory); filtration through precipitation of dust by the action of high-tension currents (an American industrial Cottrel process for the purification of smoke, proposed in France in 1938 for operating rooms by Pauthenier and Volkringer); the industrial process of "air washing" by means of antiseptic solutions (Gosset and others); the decantation of dust through a cloud of vapor (tried by Terrier a long time ago and recently vainly revived by Masmonteil in France); the hydrogen peroxide spray (Quénu, 1902); the formol treatment followed by the introduction of outside air (Flügge in Germany and Fournier in France, 1904); the use of ultraviolet rays, *etc.*, without even speaking of the initial process of Lister's carbolic acid spray (1865).

As regards the attempts at sterilization by means of water vapor under pressure, made in Italy a long time ago, it is superfluous to speak about them any further.

Sterilization by means of ultraviolet rays, which at the present time still interests a few surgeons, has seriously occupied my attention since the beginning of my investigations. I mentioned this in my first paper on the subject, in 1930 (Gudin: Presse Méd., April 15, 1930—Méthode Opératoire Stérile), saying: "As a physical agent, ultraviolet rays suggest themselves automatically, but in their connection there still are problems to be solved in order to be able to sterilize perfectly not only the air—which is easy—but also the entire surgical environment."

Finally, after all sorts of hopes, I have arrived at the firm conviction that it is in no way possible to bring about total sterilization by means of ultraviolet rays, simply because, despite all possible "cross-firing," one does not succeed in sterilizing container as well as content, a *sine qua non*. This remains an incontrovertible fact.

But ultraviolet rays, nevertheless, remain a valuable aid if—as I have done, in 1928, in the first operating room with water-tight sterilizable partitions which I built in the Gaffré-Guinle Hospital in Rio de Janeiro—one

places a series of ultraviolet lamps into the air-conditioning conduit, or if—as I am doing at the present time—one places the lamps into the air-conditioning apparatus, taking care, however, to absorb the liberated ozone by means of charcoal.

INTEGRAL ASEPSIS

The method which I have conceived for avoiding exogenous operative contamination is based upon three fundamental factors: (1) Obtaining a perfectly sterile operating room, containing all the surgical equipment; (2) employing all necessary means for avoiding the contamination of the air in this operating room and of the surgical equipment contained in the latter; (3) knowing how to execute the operation very precisely according to scientific bacteriologic principles.

The first condition is realized by the process of sterilization which I invented in 1929 and which is based on the action of chemical agents—gaseous as well as in aqueous solution—through the medium of an apparatus ("the total sterilizer") which is enclosed in a hermetically sealed operating room and electrically controlled from the outside; this apparatus can automatically maintain the conditions of temperature and humidity of the air in this room, without the introduction of outside air. This apparatus consists of several flasks containing the chemical substances, of a large pan containing a solution through which air is bubbled, and of special equipment for conditioning the air. The sterilizing agent is formaldehyde which is evaporated from a formalin solution, in amounts proportional to the size of the room, in an atmosphere saturated with moisture and vigorously agitated by powerful fans. It is obvious that no living being can enter the room which is thus saturated with this toxic agent. The latter must, therefore, be removed. This is done by the neutralization of the formaldehyde. Ammonia is evaporated in required amounts.

This substance combines with the formaldehyde in the air, and the atmosphere then contains hexamethylene-tetramine with an excess of ammonia and, therefore, does still not allow respiration.

For the removal of these chemicals from the air, the latter is bubbled through a solution of tartaric acid by means of a rotary compressor, and the air-conditioning apparatus is put into operation.

Hexamethylene-tetramine is soluble in the water, and the ammonia combines with the tartaric acid, forming ammonium tartrate, which is also soluble in water.

One thus obtains sterile air which can be freely breathed, a fact of paramount importance, on which rests the solution of the problem of integral asepsis.

Testing the Sterility of the Air.—This requires a special technic, for it is impossible to introduce agar plates into the operating room from the outside because they are contaminated and would carry in bacteria, and furthermore the aspiration of a few liters of air does not provide a sufficient guaranty.

The following test has been made and repeated a number of times: (1)

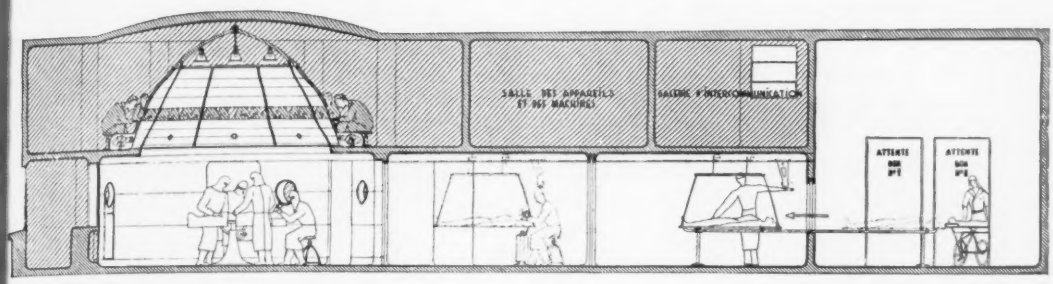

FIG. 7.—Reproduction of an internal view of the Gudin sterile operating unit, exhibited in actual dimensions, by the Surgical Academy of France at the Palace of Discovery at the International Exposition of Paris, in 1937 (*La Chirurgie*. By Gosset, Fredet, and Monod; Masson & Co., publishers).

FIG. 8.—The chemical sterilization of the surgical equipment; the wire shelves.

Agar plates are placed into the room; they are prepared in such a way that the gases do not come into contact with the agar. With this end in view, a small Petri dish containing agar is placed into a larger one not containing agar and is carefully surrounded with cotton. The whole is sterilized in the autoclave and is then placed into the room before the latter is sterilized. (2) After sterilization one enters the room, observing the precautions already described for avoiding contamination, and one opens the plates, which are then exposed for an hour or more to the powerful air currents produced by the fans. One thus circumvents the error which may arise from the existence of Trillat's droplets which, in principle, must disappear by virtue of the effect of the saturation with moisture and of the agitation of the air during sterilization. (3) The plates are now closed with the same precautions which were taken when they were opened. (4) Out of six plates, two are exposed to the outside air, in order to make sure that the formaldehyde has not penetrated and impregnated the agar. (5) Transfer to the incubator.

The result is always the same—four plates are sterile, and two are contaminated by the outside air.

The second condition: The operating room is isolated from the outside by four sterile anterooms—two for the preparation of the surgeons, and two for that of the patients—equipped with sterilizing air conditioners.

Surgeons and patients discard all their clothing before entering the sterile rooms. They are dressed in sterile overall gowns which cover the entire body, in the manner of diving-suits. The spectators are completely isolated.

The patient is brought into the room, already anesthetized, on a mobile operating table, to which the instrument trays and discard bags are attached, so that the entire unit can be evacuated as a whole to make room for the next patient.

Silence must be observed, for no mask resists if one speaks in a loud voice, or if one coughs or sneezes. No surgeons or assistants afflicted with upper respiratory infections are allowed into the room.

The hands are washed, in sterile air, with sterile hot water and sterile soap, with the aid of several successive sterile brushes, for ten minutes. Even under these conditions the hands are not sterile. The gloves remain sterile in a sterile atmosphere as long as they do not come in contact with a non-sterile object.

Sweating is prevented by conditioning the air.

The patient's skin is cleansed with benzene, and then treated for at least ten minutes with a freshly prepared 10 per cent iodine solution, which it is generally unnecessary to remove by means of alcohol.

After having resumed the study of the problem under conditions avoiding the sources of error which were inevitable with the ordinary bacteriologic methods, and having taken samples of skin, macerated them, and innoculated them into culture media in sterile air, I have arrived at the conclusion that the healthy, normal skin treated by this method is sterilized perfectly.

BRIEF COMMUNICATIONS AND CASE REPORTS

CALCIFIED INTRACEREBRAL HEMATOMA

EVERETT G. GRANTHAM, M.D.,

AND

EDMUND A. SMOLIK, M.D.*

LOUISVILLE, KY.

FROM THE DEPARTMENT OF SURGERY, UNIVERSITY OF LOUISVILLE SCHOOL OF MEDICINE, NEUROSURGICAL SERVICE OF DR. R. G. SPURLING, LOUISVILLE, KY.

THE CASE herein reported is that of a large, solitary, spherical, calcified intracerebral hematoma. In a search of the literature, we were able to find only one similar case which had been verified by operation.

Levin[1] reported the removal of a calcified mass from the left temporoparietal region which, when sectioned, showed "a laminated calcified mass, with traces of altered blood pigment, and an amorphous mass with calcifying spicules scattered in the substance. There is no evidence of tumours or of tuberculosis. The features are those of a calcified hematoma."

Case Report.—F. B., colored, male, age 46, was admitted to the Neurosurgical Service at the Louisville City Hospital, November 23, 1939, with the chief complaints of convulsions and pain in the right eye.

Present Illness.—The patient stated that when he was 13 years old he jumped from a train, stumbled, and struck his head. He was unconscious for 15 or 20 minutes. He was kept in bed at home, but was not seen by a physician. He suffered from severe headache which lasted for several days. To his knowledge there was no nausea or vomiting at the time.

About one month after the injury he had his first convulsive attack. The attacks recurred at intervals varying from one or two months apart, to as long as three years between attacks. He began the use of luminal to control the attacks in 1917.

The patient described the attacks as all beginning with a sense of nervousness. He became "faintified" and learned to lie down immediately upon the occurrence of this symptom. He then had a peculiar feeling in the left leg followed by twitching and spasm of the left leg which then progressed to the left arm and left face. Later, he lost consciousness and was told that the right side of the body had become involved. After an attack the patient suffered from frontal headache for a short time.

Since 1935, he has complained of attacks of severe pain in the right eye which radiate back toward his right ear. This has been more severe recently.

Physical Examination.—This revealed a well-developed, well-nourished, colored male, age 46, who was intelligent and cooperative. Weight 160 lbs.; temperature 98.6° F.; respiration 20; blood pressure 154/100. The general physical examination was negative except for the neurologic findings.

Neurologic Examination.—This showed a complete left homonymous hemianopsia. The pupils were equal and reacted to light. There was no choking of the optic disks or other pathology in the eyeground examination. He had good motor power in all extremities. The superficial and deep reflexes were normal, and there were no pathologic reflexes.

* Senior Assistant Resident Surgeon, Louisville City Hospital, University of Louisville, School of Medicine, Louisville, Ky.

Laboratory Data.—The urinalysis and blood count were within normal limits. The blood Kahn reaction was negative.

Roentgenologic Examination.—Roentgenograms of the skull showed a dense, sharply defined, slightly irregular shadow in the right posterior parietal area, approximately midway between the vertex and base of the skull, and approximately midway between the right lateral wall of the skull and the midline. This shadow was approximately 4 cm. in diameter and its general shape was spherical (Fig. 1).

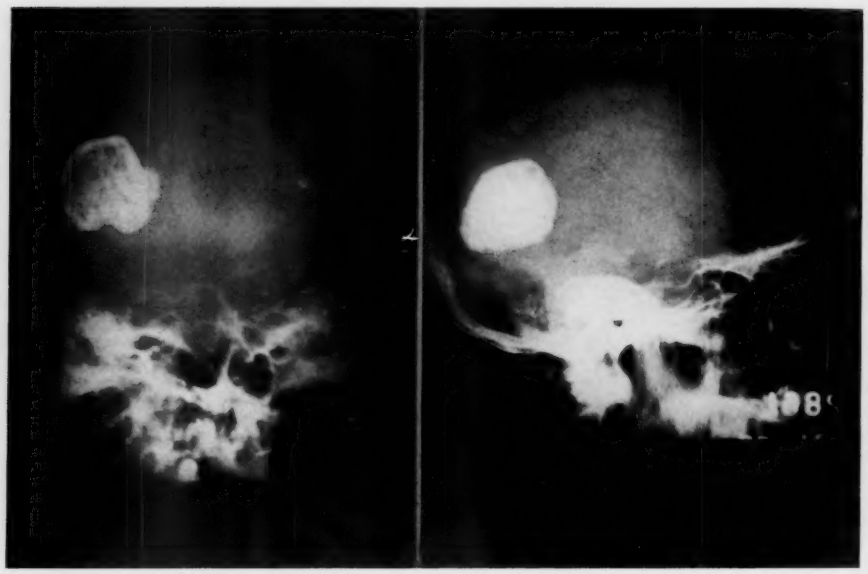

FIG. 1.—Anteroposterior and right lateral views of the skull showing the calcified mass lying in the right occipital lobe. The shadow measured approximately four centimeters in diameter.

Operation.—An osteoplastic flap was turned down in the right parieto-occipital area of the skull. The dura was under no tension and was opened along the posterior limb of the bone incision. The free edge of the dura was turned back to expose the cortex over the posterior portion of the parietal lobe and the anterior part of the occipital lobe. Inspection showed the cortex over the occipital lobe to be discolored in an area about 1 cm. in diameter. This was a brownish discoloration instead of the normal grayish appearance of the brain. Palpation of the cortex revealed a hard mass in this area which seemed to be just beneath the cortex in the region of the discolored brain and, also, under the cortex of the adjacent parietal lobe for a distance of about 3 cm. A linear incision was planned parallel with the posterior limb of the bone incision to cross the discolored cortical tissue. Silver clips were placed on two cortical vessels and a 3 cm. linear incision made in the cortex. At a depth of 1 cm. the hard dense mass was encountered. This was found intimately adherent to the surrounding brain tissue. The brain substance was gradually dissected free from the mass by the use of cotton pledgets until the deepest portion of the mass was reached. At this point the ventricle was entered while attempting to separate the mass from the brain tissue, and it was found that the mass was intimately adherent to the wall of the ventricle with only 2 or 3 Mm. of tissue separating the ventricle from the mass itself. By removing a portion of the wall of the ventricle the mass was finally freed from the brain and lifted out of its bed. The opening into the ventricle was at the junction of the posterior horn and the atrium, and a good exposure was afforded of the entire lateral ventricle.

The choroid plexus was lifted up and a silver clip placed in the vessels leading to the glomus in order to decrease the production of cerebrospinal fluid.

Pathologic Examination.—Gross: (Dr. A. J. Miller) "The specimen is a spherical mass weighing 30 Gm. The color is dull-white and the consistency is that of stone. No vessels can be found entering the mass. The mass is sectioned with a saw. There is an outer hard shell 3 to 4 Mm. in thickness. The remaining inner portion is yellowish-brown in color and semisolid in consistency, suggesting necrotic blood."

FIG. 2.—Photomicrograph of periphery of calcified mass. The capsule is an old, dense, hyalinized connective tissue, and the interior is soft grumous material resembling a necrotic blood clot. Granules of calcareous salts are widely distributed in varying density. There is no leukocytic infiltration.

Microscopically, "the inner portion stains uniformly with eosin. There are numerous strands which are evidently partly broken down fibrin. Quite a number of forms that have the appearance of cells are noted but there is no differential staining and the outlines are not definite. The structure suggests a necrotic blood clot. Here and there are small diffuse deposits of calcium. The capsule is fibrillar but it also is uniformly stained with eosin. The fibrils are arranged parallel to the surface chiefly, and this entire outer zone is quite densely infiltrated with calcium salts. The structure suggests that organization of the mass was attempted but for some reason was arrested and necrosis and calcification followed. Clinging to the outer surface are a few small masses of brain tissue. These show some gliosis and pyknosis of the glial cells. There is nothing to suggest tumor growth." *Pathologic Diagnosis:* "Hematoma, calcified."

Postoperative Course.—The patient left the operating room in excellent condition. Blood pressure 140/96; pulse 90; respirations 20. He had conversed with the attendants during the entire operation. The second day after operation the patient began to show signs of increasing intracranial pressure. This was relieved by intravenous injections of 50 per cent sucrose three times daily. Later, several spinal punctures were performed to relieve headache. The patient was discharged from the hospital three weeks after operation. He was asked to report to the Out-Patient Department for medication to prevent the recurrence of any convulsions. Here, he was given a supply of Dilantin and instructed to take 3 gr. twice daily.

SUMMARY

Large, solitary, intracerebral hematomata are not a common complication of head trauma. However, they are frequent enough to justify consideration when the patient presents focal symptoms with increase of intracranial pressure following an injury to the head. In this clinic, six such intracerebral hemorrhages have been removed surgically. Presumably, many of the smaller ones are absorbed and the patient recovers without surgical intervention. For one to become completely calcified is certainly a rare occurrence.

In the case herein reported, the history indicates clearly that the hemorrhage into the occipital lobe resulted from head trauma 33 years prior to admission. The persistent severe headache immediately following the accident followed by focal convulsions one month later is in keeping with this assumption.

We do not expect that removal of the calcified mass will cure the convulsive episodes. We are hopeful, however, that the removal will facilitate treatment in much the same way that excision of a localized cortical scar facilitates the control of convulsions. The patient will be encouraged to continue an optimal level of sodium diphenyl hydantoinate therapy over a period of years.

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HEMORRHAGE INTO THE THYROID GLAND RESULTING FROM MUSCULAR EFFORT*

REPORT OF A CASE

WILLIAM JOHN RYAN, M.D.

PHILADELPHIA, PA.

FROM THE DEPARTMENT OF SURGERY, ST. MARY'S HOSPITAL, PHILADELPHIA, PA.

ALMOST ALL adenomatous goiters removed surgically show hemorrhagic areas as well as a fibrosis, and calcareous and hyaline degeneration. Such hemorrhages, however, are probably only of pathologic interest. Even the pathologist ignores them because his interest is more in the cellular and colloid changes which are primary and related to thyroid function. Hemorrhage into the thyroid, severe enough to cause symptoms, would not appear to be a common event. A fairly comprehensive review of the literature shows very few articles on the subject. McGregor and Cornett[1] claim it is a frequent occurrence; Ballin and Morse[2] comment on its frequency, yet Schwoerer,[3] in a review of 2,500 thyroid operations, found only 18 cases of hemorrhage. Plummer,[4] and later Plummer and Broders,[5] made a search for acute, painful enlargements of the thyroid at the Mayo Clinic and found only 16 cases. Of these, in only two was the enlargement so precipitous, reaching its maximum in a few minutes, that it was attributed to hemorrhage. At operation, marked hemorrhage was found. Clute[6] states that while hemorrhage may occur in an adenoma of the thyroid it is rare. He reviewed his recent experiences at the Lahey Clinic in order to explain the alarming symptoms that sometimes occur in bad goiter cases. He cited two cases, and believes that during the last ten years they had had about six such cases.

In diagnosing the condition, malignancy must be ruled out. A good history is most important. In some cases, a tumor of the thyroid had been present for some time. In others, none had been noted. Then, on sudden physical exertion, which does not need to be necessarily heavy, pain in the neck and a sudden swelling occurred. This was usually followed by difficulty in swallowing. Abscess, though it has been reported, is even more unusual than hemorrhage.

Sometimes hemorrhage is so severe that coma and death ensue even in spite of operation. Wendel[7] reports a case of rupture of the thyroid due to great hemorrhage in "a man, age 55, who, after straining at defecation, had sudden difficulty in swallowing, became unconscious, dyspneic and died in spite of emergency surgery to remove tension." McGregor and Cornett reported a case which also died. It was a spontaneous rupture of a cystic adenoma in a woman; the hemorrhage ruptured through the capsule and infiltrated the fascial and muscle planes of the neck spreading into the mediastinum. Von Ziemacki[8] reports a somewhat similar case in a woman, with recovery. The blood extravasated anteriorly down to the level of the

* Presented before the Philadelphia Academy of Surgery, May 6, 1940.

umbilicus. A number of other isolated cases are reported but with very meager details.

Case Report.—B. C., white, male, age 45, a motor-truck driver. There was no previous history of any enlargement in the neck. He had had an appendicectomy in

FIG. 1. FIG. 3.

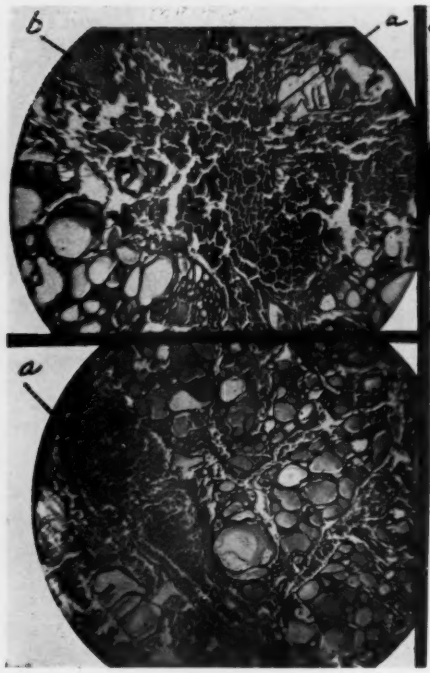

FIG. 2.

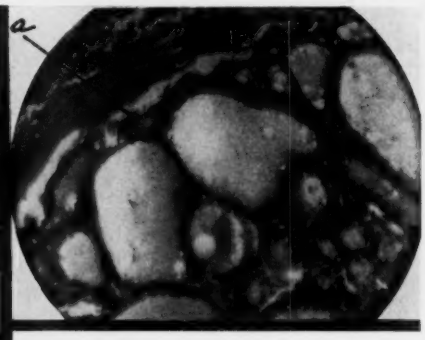

FIG. 1.—Shows massive hemorrhage, blood clots, blood pigment and serum in thyroid tissue. In upper left torn and isolated follicles in massive cloth.(a) Everywhere the hemorrhage has traversed the interlobular septa and rent them asunder. In upper right organizing clot projects as a wedge toward center of section.(b)

FIG. 2.—Shows colloid hyperplasia with giant follicle in upper center. Toward the left there is a large blood vessel containing a massive clot.(a) The walls of the vessel are not intact. Loose trabeculae of lobules appear infiltrated with hemorrhage which has separated the lobules. To the right of a giant follicle there is hemorrhage extending downward. The blood has forced the loose tissue apart.

FIG. 3.—High power view of giant follicle showing colloid hyperplasia. In upper corner there is one wall of large vessel, an interlobular artery. Notice very thick fibrotic wall lined with endothelial cells and with fibroblasts and spindle cells in the wall. This vessel does not appear to be involved in the hemorrhage. Its arteriosclerotic and brittle walls have separated or receded from the lobule producing the gaping space noted.(a)

childhood, and a fracture of the ankle about one year ago. He claimed to have always been in good health. His occupation always required moderately heavy lifting, and, occasionally, extremely heavy lifting. On August 2, 1938, while unloading bales from his truck "he felt something let go in his neck." He placed his hand there and noted a lump. His companion also noted it. He had no immediate pain but his neck felt uncomfortable and he had slight difficulty in swallowing. He was seen within a short time by his own physician and, later, was examined by another. The condition was more annoying than disabling. He stated that roentgenograms had also been taken of his neck. We first saw him August 30, 1938.

Physical Examination.—The patient was a well-developed, well-nourished, muscular individual. The first thing noted was that, although he wore a tie, he was unable to button the collar of his shirt. Examination revealed an enlargement to the left of and just below the thyroid cartilage. It moved up and down on swallowing and was not adherent to the skin. It was not tender and no bruit could be heard over it. It was smooth and was about the size of a hen's egg. Pulse 80; blood pressure 125/75. The heart action was regular and of good volume, with no murmurs present. His B.M.R. however was minus 14. *Clinical Diagnosis:* Hemorrhage into the thyroid gland or into a cystadenoma. Operation was not performed, however, until November 14, 1938—the

delay being due to whether or not this case could be considered as a compensable one. It was finally decided that it was.

Operation.—Under avertin and 2 per cent novocain, a left lobectomy was performed. A cystic adenoma was found. The cyst contained clear, straw-colored fluid and old blood. The postoperative course was uncomplicated, and he was able to return to his work about six weeks following the operation.

Pathologic Examination.—The specimen is the left lobe of a thyroid gland, with fibrotic capsule, measuring 8x5x4 cm. It contains a cyst over 3 cm. in diameter near the outer or left border. The surface vessels are prominent and tortuous. On cut-surface, considerable colloid in very fine, pinhead-size, circular follicles can be seen. Between are areas of hemorrhage several millimeters to 2 or 3 cm. in size. The cyst contains a clot, dark brown in color, 2 cm. in diameter. It also contains straw-colored fluid. There is fibrosis and arteriosclerosis of the interstitial tissues. *Pathologic Diagnosis:* (1) Interstitial hyperplasia of thyroid. (2) Massive hemorrhage into thyroid. (3) Massive hemorrhage into a cystadenoma of thyroid.

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ANOMALOUS DISTRIBUTION OF THE EXTRAHEPATIC BILIARY DUCTS

REPORT OF A CASE

CLYDE EVERETT, M.D.

AND

HAROLD E. MACUMBER, M.D.

CLEVELAND, OHIO

FROM THE DIVISIONS OF SURGERY AND PATHOLOGY OF CLEVELAND CITY HOSPITAL, AND THE MEDICAL SCHOOL OF WESTERN RESERVE UNIVERSITY, CLEVELAND, OHIO

We wish to report an unusual anomaly of the extrahepatic biliary tract that was recently encountered. A search through the literature revealed one similar but slightly different condition.

FIG. 1.—Barium study of the stomach and duodenum showing the passage of the barium into the biliary ducts.

Case Report.—N. Z., white, female, age 71, was admitted to City Hospital, January 9, 1940, complaining of abdominal pain. She gave a history of recurring attacks of indigestion for as long as she could remember, but two years before admission they became much more severe. There was no actual pain at this time, but rather a burning sensation in the epigastrium followed by bloating and belching, and later by nausea and vomiting. The attacks usually followed meals, particularly those containing fatty foods. She noticed jaundice on several occasions but never noticed clay-colored stools. Two weeks before admission she began to have severe epigastric and right upper quadrant pain with persistent nausea and vomiting. Icterus developed four days later, and had persisted to the time of admission. There had been a weight loss of 65 pounds in the last two years. There had been no other serious illness and no operations.

Physical Examination.—The patient was a well-developed but poorly nourished white woman, appearing chronically ill. The skin was loose, inelastic and definitely icteric. The sclerae had an icteric tint. There were a few wheezing râles over both lung fields. The heart was essentially normal. The abdomen was pendulous, with tenderness in the right upper quadrant, and the sensation of a mass in that region. Pelvic and rectal examination gave no additional information. Red blood count 4,250,000, with 85 per cent hemoglobin; 17,400 W.B.C. The urine showed traces of bile and an occasional pus cell. The stools were all dark brown or green. Blood urea nitrogen 8.5 mg.; icteric index 21; blood cholesterol 250. The Kline test was negative.

Roentgenologic Examination.—Studies of the gallbladder and upper gastro-intestinal tract (Figs. 1 and 2) showed several small shadows in the region of the duodenal cap,

which seemed to be due to the passage of barium into the biliary passages. The gallbladder did not visualize. There was slight spasm of the pylorus but otherwise the stomach and duodenum appeared normal. A plain roentgenogram of the abdomen showed no definite evidence of an abnormal soft tissue mass or of calculi. A roentgenogram of the chest showed the heart to be slightly enlarged.

Several diagnoses were suggested in view of the peculiar roentgenographic findings: (1) Cholecystoduodenal fistula from ulceration of a biliary stone; (2) carcinoma of the ampulla or of the head of the pancreas; and (3) chronic cholecystitis with cholelithiasis.

Operation.—Celiotomy: The gallbladder could not be found. The common duct was dilated but no stones were palpated; the duct was not opened. The stomach and duodenum appeared normal. The abdomen was closed without further procedure. The patient did not tolerate the operation well, and the course was complicated by dehiscence of the wound on the fifth postoperative day, and evisceration. She died on the fourteenth postoperative day.

Autopsy.—The liver was found to be essentially normal. A single hepatic duct emerged from each of the two lateral lobes. These joined immediately, to form a single main hepatic duct which was greatly dilated, obtaining a maximum circumference of 31 Mm. Four centimeters from the hilum of the liver this duct divided into two branches. One branch emptied into the second portion of the duodenum at the ampulla of Vater, in common with the main pancreatic duct. The other branch emptied into the posterosuperior aspect of the lesser curvature of the stomach, 1 cm. proximal to the pyloric ring. Microscopic examination at various points showed the wall to be characteristic of the extrahepatic biliary duct system, except for the distal 2.5 cm. At this point gradual transition to gastric wall occurred. No evidence of a gallbladder was found.

FIG. 2.—Oblique view showing the biliary ducts outlined by barium. In retrospect, this view shows two branches of the common duct; the one emptying into the stomach and the other into the duodenum.

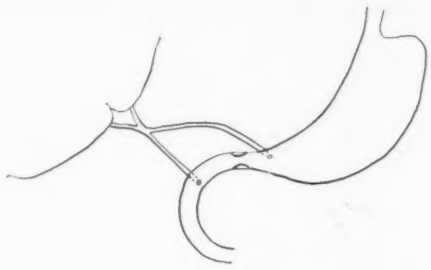

Fig. 3

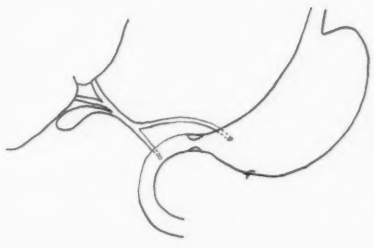

Fig. 4

FIG. 3.—Our case showing congenital aplasia of the gallbladder and high bifurcation of the common duct; one branch emptying into the second part of the duodenum, the other branch emptying into the stomach near the pylorus.
FIG. 4.—Vesale's case; similar to ours except for the presence of the gallbladder.

COMMENT.—We have been able to find only four other cases, in the literature, in which the common duct emptied into the stomach. Laennec

and Bleifuss have each reported one such case.[1] According to Owen,[2] this is the normal site of bile drainage in the bream, an European fresh water fish. Filippini described a case in which the common duct emptied into the stomach through the pylorus.[3] Vesale reported a case in which the common duct bifurcated; the upper duct emptying into the stomach above the pylorus, the lower duct emptying into the duodenum. However, the gallbladder was present in this case (Fig. 3).

Aplasia of the gallbladder has occurred three time in a series of over 13,000 autopsies recorded at City Hospital. There were no other anomalies of the common duct found in this series.

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NYLON SUTURE *

DERMONT W. MELICK, M.D.
MADISON, WIS.

THE POSSIBILITY of using Nylon as a surgical suture suggested itself when, in 1938, it was learned the DuPont Company had developed a synthetic substitute for silk. In view of the fact that many surgeons are advocates of silk it was thought Nylon might find equal favor should it have the qualities attributed to silk.

Physical Characteristics.—The physical characteristics of Nylon[1] as compared to silk are shown in Table I:

TABLE I

PHYSICAL CHARACTERISTICS OF NYLON AS COMPARED TO SILK

	Nylon	*Silk*
Relative tensile strength	1.3%	1.0%
Elongation	25.7%	12.9%
Loss in strength when wet	14.7%	24.5%
Approximate moisture content under standard conditions	3.0%	15.0%
Elastic recovery under controlled conditions	77.0%	65.0%

The Nylon suture may be obtained† either as a single strand suture, called monofilament, or a multiple strand suture, called multifilament. The multifilament looks and feels very much like silk. The monofilament is comparable to the commonly known "dermal" and "tension" suture.

Animal (dog) experimentation was resorted to in order to study the effect of various sutures (catgut and silk as well as Nylon) in relation to tissue reaction and to the process of wound healing as ascertained by gross and microscopic studies. Nylon monofilament, Nylon multifilament, silk, plain and chromic catgut were imbedded in the anterior abdominal wall of dogs, and, at intervals between two days and 103 days, biopsies were taken and paraffin sections made. Intestinal anastomoses were also performed for comparison between fine chromic catgut (No. 00000) and Nylon multifilament (No. 000).

Results.—The results obtained are graphically illustrated in Chart 1:

Clinical Use of Nylon Suture.—Following experimentation on animals it was thought Nylon multifilament was worthy of a trial in the human. It was used as a suture on a limited number (ten) of hospital patients, in the performance of inguinal herniorrhaphy only. Five different operators used the suture in order to obtain individual reactions regarding its good or bad points. The opinions voiced were favorable. It was agreed that the suture was comparable to silk in the way it handled. The greater tensile strength of the suture as compared with silk of a similar size was particularly noted by each operator.

* Abbreviated report of a thesis presented to the faculty of the Graduate School of Medicine, University of Pennsylvania, in partial fulfillment of the requirements for the degree of M.Sc. (Med) for graduate work in surgery.

† All Nylon sutures for this study were supplied by Bauer and Black, Chicago, Illinois, through the courtesy of Mr. Paul F. Ziegler, Director of Curity Research Laboratory.

Wound healing was satisfactory in all of the patients upon whom Nylon multifilament was used as a suture. The incisions presented a minimal amount of reaction. The deep fascia and subcutaneous tissue was free of the diffuse induration noted with catgut suture.

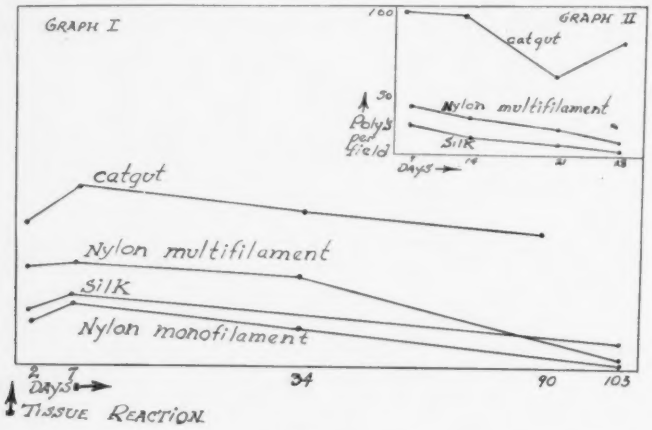

CHART 1

Graph 1 illustrates the relative reaction of the tissues to the different sutures studied. Catgut caused the most tissue reaction and Nylon monofilament the least tissue reaction.

Graph 2 (inset) is adapted from the findings of Nichols and Diack.[1] They measured the tissue reaction to suture material by the number of polymorphonuclear leukocytes found per high power field.

SUMMARY.—(1) Nylon multifilament causes less reaction in the tissues (of dogs) than does catgut. In the earlier stages of healing Nylon multifilament causes more reaction than does silk. The end-result of the healing process is practically the same for both Nylon multifilament and silk.

(2) Nylon multifilament is not completely noncapillary. Monocytes were heavily infiltrated between the interstices of the suture, when examined at the end of 34 days.

(3) Nylon multifilament is superior to silk in that it has a better tensile strength for comparable sizes.

(4) Nylon monofilament causes less tissue reaction than any of the sutures studied. It is not so flexible as Nylon multifilament, is more difficult to handle, and has a tendency to slip when tied with the usual surgical knot.

CONCLUSION

Nylon multifilament may be recommended as a satisfactory surgical suture.

Experimental and clinical studies were carried out under the supervision of Dr. E. R. Schmidt, Professor of Surgery, University of Wisconsin School of Medicine, Madison, Wis.

NOTE:—Since completion of the above report fifteen additional herniorraphies have been performed using Nylon multifilament No. 0 as the suture material. Tissue reaction has been minimal and wound healing satisfactory in all cases.

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INTRA-ABDOMINAL RUPTURE OF RETROPERITONEAL TUBERCULOUS LYMPH NODE

HIRAM O. STUDLEY, M.D.

CLEVELAND, OHIO

UNUSUAL clinical, operative, and pathologic findings in a patient who presented signs of an acute abdominal catastrophe is the occasion for the appended report:

Case Report.—R. S., white, male, age 21, was admitted to the Lakeside Hospital, stating that he had been awakened at about 6 A.M. (four hours previously) by an extremely severe, burning epigastric pain. The flexed position into which it forced him made it difficult for him to get out of bed. He became nauseated but did not vomit. Although there had been no change from the regular bowel habits, two cathartic pills were taken upon the advice of his parents. The severe pain continued and difficulty developed in breathing.

The previous history was negative except for epigastric pain for two to three hours after each meal, which was first experienced about a week before the present episode. However, this had not prevented him from eating many handfuls of peanuts on the previous day. He had felt entirely well otherwise except for a common cold of moderate severity. Abdominal examination showed board-like rigidity especially in the epigastrium. Despite the recency of the onset the temperature was 101° F. (38.2° C.). White cell count 20,000.

Physical Examination.—The patient was well-developed and well-nourished; he lay very quietly in bed as if afraid to move. His face was flushed, the respirations were rather shallow and at 28 per minute. Grunting sounds were absent and there was neither cough nor movements of the alae nasi. Severe suffering was obvious. The abdominal pain, though general, was localized by the patient as most intense in the umbilical region. The abdominal wall was splinted, and the board-like rigidity extended to the midhypogastrium, beyond which it was slightly but definitely less resistant. Maximal tenderness was also located in the region of the umbilicus. Rectal examination was negative except for moderate tenderness everywhere to high fingertip pressure.

The temperature had risen from 101° F. (38.2° C.) to 103° F. (39.4° C.) during the past two hours; the pulse rate had increased to 110 per minute. The second white cell count showed 16,000. The urine contained a slight trace of albumin, and an occasional white cell in the centrifuged specimen.

Except for evidence of moderate nasopharyngitis, the remainder of the examination was negative. As pneumonia was considered, particular attention was paid to the lungs by two observers. A roentgenogram of the subdiaphragmatic region indicated the absence of free gas in the abdominal cavity.

Evidence adequate for a diagnosis of acute peritonitis was obvious but a likely explanation for the rapid and relatively marked rise in temperature was not apparent. Neither could the height of the leukocyte count be satisfactorily correlated with a diagnosis ordinarily associated with such rapid onset, the obvious severity of the pain, and the distribution and degree of abdominal wall spasticity.

Operation.—Under general anesthesia, the peritoneal cavity was entered through a low upper right paramedian incision. A small amount of thin, turbid fluid was encountered. A culture of this was made. The appendiceal region was first inspected and a considerable amount of fluid was aspirated. No abnormality was found. The serosa was normal in appearance and, except for the fluid, no evidence of inflammation was found until the intestines were packed away from the upper abdominal structures. A few fibrin deposits were encountered on the anterior aspect of the pylorus, but the

distal end of the body of the stomach and duodenum as well as the gallbladder appeared normal. High along the edge of, but quite indistinguishable from, the gastric wall along its lesser curvature there was exposed a roughly oval, red-brown surface, approximately 6x6 cm. in size. At the upper end of this there slowly exuded about 2 cc. of thick white material from a slightly raised, deep blue conical eminence, 2 to 3 cm. in diameter. Slight pressure in exploration expressed 3 or 4 cc. more. This was removed with moist gauze and a crater-like depression surrounded by firm indurated tissue was palpated.

The inspissated material, the crater, the firm induration, and the red-brown color of old extravasated blood, which was evident in the surface layer, clearly indicated a relatively indolent process. These underlying tissue changes obviously antedated the onset of the patient's acute symptoms and probably the subacute as well.

Three mattress sutures were placed for infolding, but as the tissue was bound down and too unyielding, a flap of the great omentum was brought up over the region of the pathologic process. This maneuver, dictated by the circumstances, coincided with the advice of Braithwaite.[2] The flap was held in place by snugly tying the lower two sutures over it and by including its distal edge in the highest suture. The wound was closed without drainage.

Postoperative Course.—All signs of peritonitis disappeared, but clinical and roentgenologic evidence of a widespread pneumonitis developed. The patient died on the third day.

Autopsy.—Limited to the abdomen and chest: Performed at the Institute of Pathology by Drs. C. C. Couch and E. S. Ingraham, Jr. Dr. Howard Karsner kindly reviewed the material. There was widespread, confluent bronchopneumonia. There was no evidence of general peritonitis. Caseous tuberculous and calcified lymph nodes of the celiac group were found. The center of one of the nodes in the gastrohepatic ligament was partially liquefied, and one wall of it had been replaced by omentum firmly attached (that placed at operation). Formalin introduced into the esophagus was made to distend the stomach and duodenum, without leakage at any point. Careful examination of the gastric and duodenal mucosa and of the mesenteric nodes of the small and large bowel showed no abnormality.

The liver and spleen contained several hard, yellow nodules 1 to 3 Mm. in diameter, which were probably, but not proven to be tuberculous.

Histologic Examination.—The celiac nodes were demonstrated to be almost entirely replaced by large and small nodules composed of broad fibrous borders, surrounding granular and frequently basophilic amorphous centers. In the open node (covered by omentum), an unusually large caseous center was present, together with a small amount of fresh granulation tissue, heavily infiltrated with lymphocytes, plasma cells, and a few polymorphonuclear leukocytes. In this region, were several small active tubercles composed of young endothelioid cells; a few contained small necrotic centers. Associated with the tubercles were several giant cells of the Langhans' type.

The adjacent serous surfaces showed a thin layer of fibrin enmeshing moderate numbers of lymphocytes and granulocytes. In some situations there was early organization of this exudate. Examination of the gastro-intestinal tract was negative, and sections of the bowel remote from the pylorus showed a thin, normal serosa. Culture of the peritoneal fluid resulted in no growth after six days.

Review of the roentgenograms of the upper abdomen showed several large calcified nodes in the central portion. In the region of the spleen, there were numerous shadows of the density of calcium, about 3x3 Mm. in size, which, probably, represented calcified tuberculous foci in that organ (Fig. 1).

COMMENT.—Among the large number of cases of abdominal tuberculous lymphadenopathy reported in the literature, the descriptions of a few cases of ruptured lymph nodes were found: Iselin[6] reported six; Newboldt[7] reported

two; Colt and Clark[3] one; Head[5] one; and four cases were referred to in Anderson's[1] series.

The outstanding findings in the case presented herewith were: Preoperatively, extreme pain of rapid onset, abdominal wall rigidity, an early and extensive rise in fever, and a high leukocytosis. At operation, minimal evidence of general peritonitis which was limited to a moderate amount of free serous

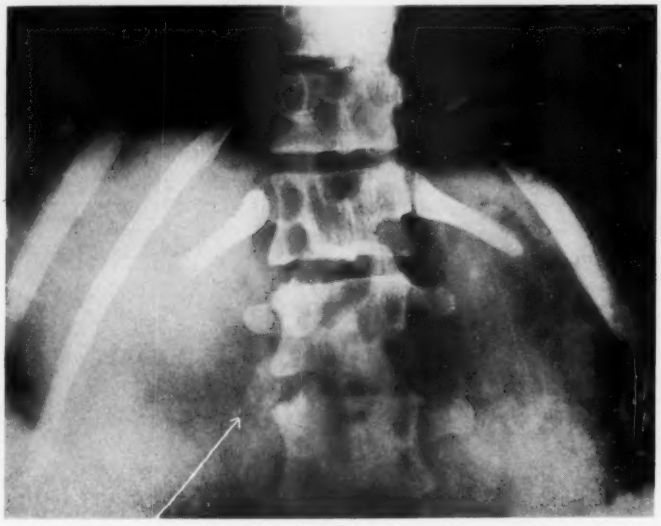

FIG. 1.—Roentgenogram showing multiple areas of increased density in the region of the spleen, and in the central portion of the upper abdomen.

fluid, and the regional deposits of a few flakes of fibrin; visceral peritoneum of normal appearance save in the lesser omentum about the ruptured abscess. Postoperatively, disappearance of signs of peritonitis, and only slight and local evidence of such at autopsy.

In interpretation, the discomfort during the week prior to the acute episode was correlated with the regional inflammation about the retroperitoneal tuberculous lymph node abscess. In two cases of rather large retroperitoneal tuberculous lymph node masses, described by Ravdin,[8] pain was not a prominent complaint.

The board-like abdominal rigidity and the extreme pain, best described as agony, indicated the presence of a substance in the released contents of the tuberculous abscess which was extremely irritant to the parietal peritoneum. In a case of ruptured tuberculous lymph nodes in the ileocecal region, reported by Head, the peritoneal irritation was evidently comparably intense, as the pain was sufficient to cause the patient, a young adult male, to "double up and roll on the floor." Rigidity in the abdominal wall was also found.

The early advance in fever was consistent with the observation of Fraser[4] that "fever introduces the illness in cases of acute tuberculous lymphadenitis"; also, with that of Braithwaite who considered a fever over 100° F. (38.0° C.) as suggestive of this disease rather than of appendicitis.

Rupture of the tuberculous abscess of the celiac group of nodes into the upper abdominal cavity resulted in a process which was, evidently, an unusual type of acute nonpyogenic, or of an aseptic peritonitis. The process was notable, not only for the evident intensity of the stimulation of the sensory elements of the parietal peritoneum but, also, for its prompt and marked general systemic effect. The unusual combination of considerable early fever and very severe abdominal pain, with rigidity, may serve as clarifying evidence in the preoperative diagnosis in the rare case of free rupture of a tuberculous abscess into the general peritoneal cavity.

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